1.0 Abstract

Title

Post-Marketing Surveillance of Synagis in Korean Pediatric Patients under the "New Drug Re-Examination"

Keywords

Respiratory syncytial virus (RSV), Synagis, palivizumab, Post marketing surveillance

Rationale and Background

This surveillance was being conducted in compliance with the Korean regulations on New Drug Re-examination. The purpose of the New Drug Re-examination is to observe the type and incidence of unexpected (newly identified) adverse events and factors affecting safety of the new drug in Korean population, so that the regulatory authority could do the post-marketing authorization management properly.

Research Question and Objectives

The objective of this surveillance study is to evaluate the following items in relation to the use of Synagis (palivizumab) in routine medical practice settings in Korea:

1. Serious adverse events and serious adverse drug reactions
2. Unexpected adverse events and unexpected adverse drug reactions
3. Known adverse drug reactions
4. Non-serious adverse drug reactions

Study Design

Non Interventional, prospective, multi-center, post marketing observational study in Korea.

Setting

The use of Synagis in routine medical practice settings in Korea.

Subjects and Study Size, Including Dropouts

According to the regulation, Synagis (palivizumab) is a product that is mandated to collect information on a total of 600 or more Korean pediatric subjects over a period of up to 6 years.

Variables and Data Sources

Variables and data sources to be collected include pertinent subject background information, e.g., demographics, background characteristics, details on Synagis prophylaxis, previous/concomitant medication, concomitant treatments, lower respiratory tract tnfection (LRI) and adverse events.

Results

Safety analysis was performed with data from 617 subjects. Thirty-five investigators from 29 investigational sites participated in the present study.

Mean (SD) age at enrollment was 3.38 (3.39) months. Mean (SD) gestational age was 31.46 (4.91) weeks, and mean (SD) birth weight was 1.68 (0.89) kg. 444 subjects (444/617, 72.79%) had premature births (less than or equal 35 weeks gestation) and 336 of 617 subjects were male (54.56%).

The most common indication for Synagis administration was indication 1 of preterm newborn infants or infants born at 35 weeks of gestation or less, and less than 6 months of age at the onset of RSV season (347/617, 56.24%). 21.39% of infants who received Synagis had BPD and 32.09% had CHD.

Concomitant medications were used by 69.04% of subjects. According to pharmacological subgroup, the most common medications were diuretics (23.01%). Concomitant treatments with the exclusion of pharmacological interventions were

given to 25.12% of subjects. Mechanical ventilation was most frequently used concomitant treatment (92 subjects among 155 subjects who were given concomitant treatments).

Mean (SD) Synagis dose administered per subject throughout the study was 14.81 (1.82) mg/kg.

A total of 380 (61.59%) subjects received 4 (8.27%) or 5 (53.32%) doses of Synagis and 237 (38.40%) subjects received less than 4 doses of Synagis. 154 subjects received incomplete RSV prophylaxis as prescribed by their physicians. Two subjects discontinued because of a RSV infection and 4 discontinuations due to adverse events (AEs) occurred (2.59% of discontinuations). Thirty-seven subjects (24.03% of discontinuations) withdrew from study. Of the other reasons for Synagis discontinuations (72.08%), financial consideration due to injection cost with improvements of subjects' underlying conditions, and transfer to other hospitals were the main reasons except for 1 case of death, and in 13 cases the reasons were unknown.

Twenty-seven subjects (27/617, 4.38%) experienced LRI. Their mean (SD) hospital stay was 15.85 (18.39) days. Subjects with moderate to severe lower respiratory infection (LRI score is 3 or greater) were 19 among these 27 subjects (19/27, 70.37%). RSV antigen tests done for evaluation of the respiratory illness were positive in 15 subjects (15/27, 55.56%).

A total of 126 subjects (20.42%) reported 213 adverse events and 3 AEs related to Synagis (ADRs) were reported. According to primary system organ class (SOC), AEs concerning the infections and infestations SOC were the most commonly reported (114 AEs in 82 [13.29%] of the subjects) and the AEs by preferred term (PT) that were reported ≥ 1% of incidence during the study were upper respiratory infection (32 subjects, 5.19%), pyrexia (16 subjects, 2.59%), bronchiolitis (13 subjects, 2.11%), respiratory syncytial virus infection (11 subjects, 1.78%), and diarrhea (8 subjects, 1.30%). In total, 3 AEs (3/213, 1.41%) were reported as related to Synagis.

Forty-six subjects (46/617, 7.46%) reported 60 SAEs and 3 SAEs related to Synagis (serious ADRs) were reported. According to SOC, SAEs concerning the infections and infestations were the most commonly reported (38 SAEs in 31 [5.02%]) of the subjects. The most common SAEs by preferred term (PT) during the study were respiratory syncytial infection (11 cases from 11 subjects, 1.78%).

99 cases of Unexpected AEs (i.e., AEs not printed in the Korean label) from 67 subjects were reported but, none of these AEs was assessed to be related to Synagis by site investigators.

Six SAEs from 5 subjects have been reported as 'Fatal/Death.' The PTs of SAEs related to these fatal events were 'Cardiac failure,' 'Bacteraemia' from 1 subject and 'Death' from 1 subject, 'Chronic respiratory failure' from 2 subjects, 'Condition aggravated' from 1 subject, respectively. However, all of these deaths were not attributed to Synagis by the study investigators.

Discussion

This study observed the safety profile of the indicated use of Synagis in Korean subjects. The adverse events reported generally reflected the serious underlying conditions of the pediatric subjects receiving Synagis or are not unexpected for Synagis. There was no new safety signal identified from the results of this study.

Marketing Authorisation Holders

AbbVie Korea

Names and Affiliations of Principal Investigators

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