A Postlicensure Evaluation of the Safety of Live Attenuated Influenza Vaccine in Children 2 to 4 Years of Age

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Background

• In 2007, MedImmune committed to conduct a postlicensure evaluation of the safety of LAIV in children 2-4 years of age.

Objective

• To describe the incidence of medically attended events (MAEs) following LAIV administration among eligible children 24-59 months of age.

Methods

• Two independent reviews of LAIV in Kaiser Permanente Northern California as part of routine care from October 2007 through March 2010 and were monitored afterward using their healthcare database.

• MAEs in LAIV recipients were compared with rates in 3 different nonrandomized controls; a self-control, unvaccinated controls, and TIV recipients.

• Subjects were enrolled at age 24 and 35.

• For each cohort group, rate comparisons were made for each postvaccination period (21, 42, or 165 days) and setting (Kaiser, emergency department, and hospital).

• MAEs through 42 days postvaccination and hospitalizations/deaths through 180 days postvaccination were analyzed.

• Individual dose events were performed for specific diagnoses of interest.

• MAEs were also pooled together in 11 subgroups and calculated alongside summary rates all settings as preplanned.

• There included 20 respiratory tract events, 10 cutaneous/podiatric tract events, 2 gastroenteritis, 1 dermatological, 2 soft tissue, and 6 event type-related to no type assigned.

• Individual MAEs and PSDIs that were significantly increased or decreased after vaccination with LAIV were organized by age group in a hierarchical data map [Figures 1 and 2].

• MedDRA was assigned without multiplicity adjustment.

Results

• 23,462 LAIV recipients were enrolled at 36.8% TIV recipients and 44,963 unvaccinated subjects (Table 2).

• Of the 246,891 dose comparisons, 86 and 57 comparisons at a significantly higher and lower rate, respectively, after vaccination with LAIV. 177 significant comparisons were identified from individual MAEs (Figure 3) and were not from PSDIs (Figure 4). For the within-cohort comparisons, 60 were statistically significant, of which 13% comparisons occurred during the higher rate during the postvaccination period in the reference period.

• For the unvaccinated controls, 140 comparisons were statistically significant, of which 60% (60) comparisons occurred at a significantly higher rate in LAIV recipients relative to unvaccinated controls.

• For the TIV controls, 143 comparisons were statistically significant, of which 35% (35) comparisons occurred at a significantly higher rate in LAIV recipients relative to TIV recipients.

• Only events within 21 days of vaccination occurred at a significantly higher rate after LAIV in comparison to unvaccinated children and TIV recipients.

• Among 20 respiratory tract events, only 5 occurred at a significantly higher rate after vaccination with LAIV and were in comparison with unvaccinated children.

• No dangerous events occurred within 21 days postvaccination.

• A total of 15 serious adverse events (SAEs) within 42 days of vaccination occurred in 20 LAIV recipients.

• 2-A year note was noted subsequent tight control of presence 6 days after vaccination with LAIV and a total of 18 events were demonstrated with deaths in the reference period.

• No SAE occurred at a significantly higher rate among LAIV recipients.

• No deaths occurred among LAIV recipients throughout the study.

Conclusion

• The results of this postlicensure evaluation of LAIV safety in US children 2-4 months of age are consistent with preappraisal clinical studies and Vaccine Adverse Event Reporting System reports, both of which demonstrated no significant increase in asthma and wheezing events or other adverse outcomes of severe illness in children who received LAIV.

References


Figure 1. Statistically Significant Differences in Individual MAEs in LAIV Recipients Relative to Controls in Subjects 24-60, 36-59, and 24-59 Months of Age

Figure 2. Statistical Differences in Preappraised Diagnoses of Interest in LAIV Recipients Relative to Controls in Subjects 24-36, 36-59, and 24-59 Months of Age