Cold-Adapted Nasal Flu Vaccine Shows Promise

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ATLANTA — Medimmune's investigational cold-adapted trivalent influenza vaccine appears to have a highly favorable risk-benefit profile in children aged 12-59 months without a history of wheezing, Dr. Robert Walker said at the fall meeting of the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention.

The cold-adapted influenza vaccine, trivalent (CAIV-T) is Medimmune's next-generation intranasal influenza vaccine. Unlike its currently licensed live-virus intranasal influenza vaccine, Flumist, CAIV-T does not need to be kept frozen and may be stored at 2°-8° Celsius in a refrigerator, said Dr. Walker, vice president of clinical development at Medimmune.

The company has submitted a biologics licensing application to switch formulations from Flumist, currently approved for healthy individuals aged 5-49 years, to CAIV-T for the same population. It also is seeking an expanded label for CAIV-T in children aged between 12 and 59 months without a history of wheezing. A Food and Drug Administration response is expected in the second quarter of 2007. Pending a positive outcome, Medimmune plans to commercially provide CAIV-T for the 2007-2008 influenza season, according to a company statement.

At the ACIP meeting, Dr. Walker presented pivotal data from a double-blind, multinational study in which 8,475 children aged 6-59 months were randomized to receive two doses of either CAIV-T or the injected trivalent influenza vaccine (TIV). All first doses were given by Oct. 29, 2004.

From Nov. 1, 2004, through June 1, 2005, the overall attack rate of all influenza strains was 3.9% among the CAIV-T recipients, compared with 8.6% among the children who received TIV, a significant 54.7% improvement in efficacy. Attack rates also were significantly lower with CAIV-T for the H1N1 strain (0.1% vs. 0.7%) and for H3N2 (0.9% vs. 4.5%), while the difference in attack rates of influenza B was not significant (2.9% vs. 3.5%).

Runny and/or stuffy noses were reported more often with CAIV-T, while injection site reactions were more common with TIV. Among children younger than 2 years, medically significant wheezing was significantly more common within 42 days after the first dose among the CAIV-T group, occurring in 3.2%, compared with 2.0% of the TIV recipients at weeks 2, 3, and 4 after immunization. Those rates were not different after 42 days or after the second dose, he said.

Using CAIV-T instead of TIV in a nonwheezing population would result in about 1.5 million fewer cases of symptomatic influenza annually.

Hospitalization associated with medically significant wheezing occurred in 0.3% with CAIV-T and 0.2% with TIV, with mean durations of 4.5 days and 4.0 days, respectively. There were no deaths, and no patient required intensive care or a ventilator. Recurrences of medically significant wheezing occurred in 32% of CAIV-T recipients and in 28% with TIV.

All-cause hospitalization was significantly greater with CAIV-T only in children aged 6-11 months (6.1% of 684 patients, compared with 2.8% of 683 who received TIV). The most common reasons for hospitalization were lower respiratory tract infections and gastrointestinal problems (frequently rotavirus), Dr. Walker noted.

In children with a history of wheezing, those aged 12-47 months in the CAIV-T group had significantly higher hospitalization rates than did those in the TIV group. In the 12- to 23-month age group with a history of wheezing, for example, 5.1% of the CAIV-T recipients compared with 2.6% of TIV patients were hospitalized.

However, among the children aged 12-59 months who did not have a history of wheezing, there were no differences in hospitalization rates between the CAIV-T and the TIV recipients. Similar reductions in influenza rates were seen with CAIV-T compared to TIV in the groups with and without wheezing, Dr. Walker reported. About 80% of children aged 12-59 months have no history of wheezing. Using CAIV-T in that population instead of TIV would result in about 1.5 million fewer cases of symptomatic influenza annually, he said. ■

Pages 22a—22b