

PCV13 Is Promising Against Worrisome Serotypes

BY HEIDI SPLETE
Senior Writer

WASHINGTON — An updated pneumococcal conjugate vaccine containing 13 different bacterial strains appears to be safe and immunogenic, based on pilot data from four European studies including several hundred infants and toddlers.

The data were presented in a poster session at the jointly held annual Interscience Conference on Antimicrobial Agents and

Chemotherapy (ICAAC) and the annual meeting of the Infectious Diseases Society of America (IDSA).

“Globally, the pneumococcus has been estimated to account for around 1 million deaths annually in children less than 5 years old,” stated Dr. Dorothee Kieninger of Johannes Gutenberg University in Mainz, Germany, and colleagues.

Data from the Centers for Disease Control and Prevention in Atlanta have shown a significant decrease in pneumococcal

disease in U.S. children thanks to the 7-valent pneumococcal conjugate vaccine (PCV7). But outbreaks of disease in recent years have been linked to bacterial strains not included in this vaccine, particularly serotype 19A, according to the CDC.

The studies presented at the meeting showed that the new vaccine appeared to generate an immune response with few adverse effects, but it must earn approval from the Food and Drug Administration before it can be licensed and distributed.

In Dr. Kieninger’s study, 604 healthy 2-month-old infants in Germany were randomized to receive PCV7 (303 infants) or the new vaccine PCV13 (301 infants). The children received the pneumococcal vaccines in addition to a combined diphtheria, tetanus, and acellular pertussis (DTaP) vaccine, inactivated polio vaccine (IPV), *Haemophilus influenzae* type b polysaccharide PRP (Hib), and hepatitis B surface antigen (HBsAg) (GlaxoSmithKline’s Infanrix hexa). They received the vaccinations at 2, 3, and 4 months, and again at 11-12 months. Blood samples were taken after the infant series at 5 months, and again after the toddler vaccination at 12-13 months.

The researchers compared adverse events and assessed immune responses to the seven serotypes in PCV7 (4, 6B, 9V, 14, 18C, 19F, and 23F) and the six additional strains in PCV13 (1, 3, 5, 6A, 7F, and 19A).

Overall, antibody responses to the PCV7 serotypes were similar in both groups. But for the six additional serotypes in PCV13, the functional antibodies were 10-100 times higher in the PCV13 group, compared with the PCV7 group.

The positive antibody response of 19A is of particular interest, given the increased incidence of pneumococcal disease caused by this serotype, Dr. Christine Juergens of Wyeth Research in Muenster, Germany, said in an interview.

The primary measure of immunogenicity in this study and the other PCV13 studies presented at the meeting was the proportion of children who achieved an antipolysaccharide IgG binding concentration of at least 0.35 mcg/mL. For 19A, this percentage was 99% in the PCV13 group.

The lack of interference from concomitant vaccines in the safety and effectiveness of PCV13 also is important, said Dr. Juergens, a coinvestigator for the study.

No clinically meaningful differences in safety or tolerability were observed between the two groups, the researchers said, and no severe adverse events were reported in either group in response to the infant dose. One incidence of febrile convulsion occurred in one toddler in the PCV7 group.

But there were some significant differences in local reactions between the PCV13 and PCV7 groups. Patients who received PCV13 compared with PCV7 reported significantly more induration (28% vs. 21%) but significantly less erythema (28% vs. 36%) after the first dose, and significantly less induration (27% vs. 35%) and erythema (34% vs. 47%) after the second dose. In addition, there was a significantly greater incidence of mild fever after the third dose in the PCV13 group, compared with the PCV7 group (46% vs. 37%) but there was a significantly lower incidence of sleepiness after the second dose in the PCV13 group, compared with the PCV7 group (54% vs. 67%).

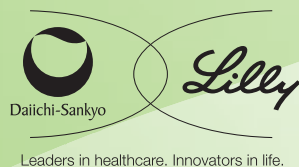
Data from another study of a three-dose infant vaccination series showed similar safety and immunogenicity results for PCV7 and PCV13 when each vaccine was given along with a DTaP, IPV, and Hib vaccine (Sanofi Pasteur’s Pentavac). This study was conducted in France by Dr. Emmanuel Grimprel of the Armand Trousseau Hospital in Paris, and colleagues.

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Few Children Younger Than Age 2 Years Receive Influenza Vaccination

BY SHARON WORCESTER
Southeast Bureau

ATLANTA — Influenza vaccination rates remain low among children aged 6-23 months, despite a recommendation made 3 years ago by the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices that children younger than age 2 years be vaccinated.

The latest data show complete coverage of only about 21% in this age group, Dr. Anthony Fiore of the CDC reported at the committee's fall meeting. "We still have a long way to go," he said.

The findings are from the 2007 National Immunization Survey and are based on the 2006-2007 influenza season (MMWR 2008;57:1039-43). Data emerging from the 2007-2008 season appear similar to those from 2006-2007, Dr. Fiore noted.

Because children younger than age 2 years are at the greatest risk for influenza-related hospitalizations, ACIP in 2002 encouraged vaccination of this population, and in 2004 strengthened their stand by recommending vaccination.

According to the MMWR report, 32% of children aged 6-23 months received one or more doses of vaccine during the 2006-2007 flu season, and only 21% were fully vaccinated. Two doses given 4 weeks apart are recommended in children younger than age 9 years who are being vaccinated for the first time.

And there was substantial variability in vaccination coverage among states, according to the survey results. For example, in Mississippi, only about 9% of children were fully vaccinated, whereas in Rhode Island, nearly 48% were vaccinated. In most states, there was no significant increase in the percentage of children who were

fully vaccinated, compared with the previous flu season. "The findings underscore the need to increase interest in and access to influenza vaccination for more children in the United States. Further study is needed to identify knowledge deficits or logistical barriers that might contribute to continued low influenza vaccination coverage among young children," the article states.



With coverage at 21%, "we still have a long way to go," to vaccinate children aged 6-23 months, said Dr. Anthony Fiore.

The authors also stated in an editorial note that health care providers can help improve vaccination coverage among young children by routinely informing parents about the "burden of influenza illness among young children and about the benefits and safety of preventing influenza with vaccination."

They noted that proven strategies for reducing missed opportunities for vaccination include having standing orders to offer vaccine to all patients throughout the flu season, holding vaccination-only clinics, and using reminder/recall systems. ■

Counsel on Quitting

Smokers from page 1

coccal disease, the analysis showed.

The inclusion of smoking as an indication for vaccination provides physicians with an additional opportunity to counsel patients about the importance of smoking cessation, several committee members noted.

In addition to voting in favor of adding smoking to the list of conditions that are indications for adults aged 19-64 years, the committee also agreed to revise the wording approved in June about asthma as an indication for pneumococcal vaccination. The age group for vaccination was corrected from 18-64 years to 19-64 years to prevent overlap with the adolescent immunization schedule.

In other business related to the 23-valent pneumococcal polysaccharide vaccine (PPV23), ACIP addressed revaccination with PPV23 following prior vaccination with the 7-valent pneumococcal conjugate vaccine (PCV7) in American Indians and Alaska Natives, who may have high rates of invasive pneumococcal disease.

Vaccination is currently recommended in all American Indians and Alaska Natives aged 2-64 years. The current recommendation to use PPV23 in a large proportion of these populations is a strength, according to the authors of proposed changes to the recommendation—a group that included representatives from the Indian Health Service, the Alaska Native Tribal Health Consortium, the CDC Arctic Investigations Program, and the Johns Hopkins Center for American Indian Health—but they also noted several weaknesses. Namely, risk levels are not equal among all American Indians and Alaska Natives (increased risk data are limited to Alaska Natives, White Mountain Apache, and Navajo populations, and risk and health disparities vary by age strata); the language lacks specificity and is seen as offensive by some members of these populations; and the age group is overinclusive, they argued.

ACIP approved the group's proposal that PPV23 be recommended only for those members of the American Indian and Alaska Native populations who are younger than age 65 years and have underlying medical conditions that are PPV23 indications, or—in those aged 50-64 years—when they live in areas deemed by public health authorities to pose an increased risk of invasive pneumococcal disease. ■

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Overall, the immune responses to the concomitant antigens for a three-dose infant series were similar between a group of 266 healthy 2-month-olds who were randomized to receive PCV13 and 263 who received PCV7. The infants were vaccinated at 2, 3, and 4 months of age, and blood samples were taken at 5 months to measure immune response.

After dose 3 of the infant series, the pneumococcal immune response rate in the PCV13 group was at least 72% for all serotypes and 98% for 19A. Antibody response rates to the concomitant vaccine ranged from 59% to 100% in the PCV13 group and 63% to 100% in the PCV7 group.

In this study, as in other studies, the incidence of adverse events including injection site tenderness, erythema, and induration were not significantly different between the two groups.

The results from the French study were mirrored in a similar study conducted by Dr. Chaamala Klinger of the University of Oxford (England), and colleagues. This study included data from 135 infants aged 6-14 weeks who were randomized to receive PCV13 and 132 infants who received PCV7. Infants in both groups received the meningococcal serotype C vaccine at 2 and 4 months of age, and the pneumococcal conjugate vaccine, plus a DTaP, IPV, and Hib vaccine at age 2, 3, and 4 months.

Overall, 79%-96% of the children who received PCV13 met the criteria for protection against the six serotypes not included in PCV7,

and 95% met the criteria for protection against 19A. "PCV13 was immunogenic and well tolerated when given as part of the UK infant vaccine course," the researchers wrote.

Local reactions including tenderness, induration, and erythema were similar between the two groups, as were systemic reactions.

A study of the safety and immunogenicity of PCV13 when it was produced on a manufacturing scale supported the results from the three pilot studies.

In this study, conducted by Dr. Janusz Gadziowski of the Poznan (Poland) University of Medical Sciences, and colleagues, 134 healthy 2-month-olds were randomized to receive the PCV13 pilot vaccine and 135 received the PCV13 manufacturing scale vaccine.

The infants in each group received the PCV13 along with a DTaP, IPV, Hib vaccine, and a hepatitis B vaccine. The infants were vaccinated at 2, 3, and 4 months of age, and the researchers took blood samples at 5 months to test for immune response.

Overall, the proportions of responders who met the criteria for immunogenicity and geometric mean concentration were similar in both groups. For serotype 19A, both groups achieved identical response rates of 99%.

Adverse events were mostly mild or moderate and the investigators considered them unrelated to vaccine. Only one serious adverse event (a case of inconsolable crying) was considered vaccine related, they said. All four studies were supported by Wyeth, a manufacturer of PCV13. ■

S. pneumoniae Serotype 19A Tied To Necrotizing Pneumonia in Kids

Serotype 19A of *Streptococcus pneumoniae* is the culprit behind some complicated cases of necrotizing pneumonia in young children, based on findings from four cases that occurred between Sept. 7, 2007, and March 30, 2008, at a single hospital.

"Severe necrotizing pneumonia caused by this serotype had not previously been reported in children," said Dr. Susan Wootton of the University of Texas, Houston, who presented the cases with her associates in a poster at the jointly held annual meeting of ICAAC and IDSA.

The 19A strain is one of several that are not included in the current pneumococcal conjugate vaccine, PCV7. Data from the Centers for Disease Control and Prevention that also were presented at the meeting showed an increase in invasive pneumococcal disease from nonvaccine serotypes in all age groups.

The patients ranged in age

from 3 to 4 years (mean age, 3.4 years). Three were previously healthy and one had asthma. All four had been vaccinated with PCV7. *S. pneumoniae* was isolated from pleural fluid in three cases and from blood in three cases.

Chest radiographs revealed multilobar infiltrates in four children, empyema in three, and pneumatoceles in two. Three children were admitted to the intensive care unit and intubated 5-22 days. Three children had abscesses that required surgical drainage. The hospital stays ranged from 11 to 28 days.

Serotype 19A has not previously been reported as a cause of complicated pneumonia in children, but these cases suggest that it should now be considered in the differential diagnosis, Dr. Wootton and her associates noted. The results support the need for an expanded pneumococcal vaccine, they said.

Dr. Wootton had no financial conflicts to disclose.