Gardasil 96% Effective Against Premalignancies

BY BRUCE K. DIXON
Chicago Bureau

CHICAGO — The quadrivalent human papillomavirus vaccine, which protects women against HPV types 6, 11, 16, and 18, also prevents the abnormal growth of precancerous cells in the cervix associated with these four common types.

This finding, from the international phase IIb/III Quadrivalent HPV Vaccine Study, was reported at the annual International Conference on Antimicrobial Agents and Chemotherapy.

These premalignancies, known as cervical intraepithelial neoplasia (CIN), are a major contributor to healthcare costs resulting from screening, research, and treatment. Dr. Sven-Eric Olsson said at the conference, which was sponsored by the American Society for Microbiology.

Through 3 years of follow-up, the vaccine was 96% effective in preventing CIN related to HPV types 6, 11, 16, and 18, and vaccine efficacy was significant for all four of the HPV types. The results were somewhat less so for HPV 11, said Dr. Olsson, with the Karolinska Institute at Danderyds Hospital in Stockholm.

The Food and Drug Administration-approved quadrivalent HPV vaccine (Gardasil, Merck Co.) is recommended by the Centers for Disease Control and Prevention for use by women aged 9-26 years. The four targeted HPV types are responsible for 70% of cervical cancers and 80% of genital warts, according to the CDC.

The investigators drew data from more than 18,000 women aged 16-26 years who were enrolled in one of three randomized trials sponsored by Merck.

The cohort of women was evenly divided to receive either vaccine or placebo at day 1, month 2, and month 6. Subjects underwent cervical sampling at day 1 month 7 and Pap testing at day 1 and 6-12 month intervals for up to 48 months.

All of the specimens were HPV typed and histologically diagnosed by four blinded pathology panel, said Dr. Olsson. Merck has given the vaccine, but has no financial stake in either Merck or GlaxoSmithKline, which has filed with the FDA for approval of Cervarix, a bivalent HPV vaccine protecting against types 16 and 18.

Primary per protocol vaccine efficacy analysis included subjects who received all three of the doses, were sero- and PCR-negative to the four HPV types at day 1 and PCR negative through month 7, and had no major protocol deviations.

Dr. Olsson reported that in the group that received the vaccine, there were 6 cases of HPV 6/11/16/18 CIN, compared with 148 cases in the placebo group, providing the vaccine efficacy of 96%.

And for CIN (grade) 2 or worse, including adenocarcinoma in situ, there was 1 case in the vaccine group and 76 cases in the placebo arm, for a 99% efficacy rate,” he said, adding that vaccine efficacy was 95.9% with 148 cases in the placebo group, providing the vaccine efficacy of 96%.

“We encourage the rapid recommendation of vaccination in young adult and adolescent women,” they wrote.

In women who test positive for human papillomavirus DNA, the bivalent HPV16/18 vaccine does not induce or accelerate clearance of the infection, according to a phase III study. Human papillomavirus (HPV) vaccination induces cell mediated immune responses that are traditionally involved in the eradication of infection, and it has been suggested that the vaccine might benefit women who are already infected, perhaps by enhancing viral clearance. Researchers examined the issue using a cohort drawn from a large, ongoing randomized clinical trial of vaccine efficacy.

The subjects in the main study of vaccine efficacy were nearly 7,500 women aged 18-25 years who resided in Costa Rica, where cervical cancer screening programs incorporate HPV DNA testing along with Pap tests. “Because current management protocols often involve retesting HPV-positive women within 6 months of an initial HPV positive result before treatment decisions are made, understanding the impact of vaccination on cervical clearance in the first 6-12 months following an initial HPV positive result would be informative,” wrote study investigators Dr. Allan Hildesheim of the National Cancer Institute, Rockville, Md., and his associates.

The investigators assessed viral clearance in a subset of 2,053 subjects who were positive for HPV DNA and received either a control immunization or the bivalent HPV16/18 vaccine that contains viral particle only from HPV 16 and 18. This formulation has been approved for use in Australia and is under review for use in the United States and other countries, they noted.

Clearance rates for HPV16 and/or HPV 18 were not significantly different between the active treatment and placebo treatment groups either 6 months after the initial vaccination was given (33.4% vs. 31.6%) or at 12 months, when the entire series of vaccinations was completed (48.8% vs. 49.8%). In addition, there was no evidence of a vaccine effect in any of several subgroups studied.

The trial was funded by the National Cancer Institute and the National Institutes of Health. Although HPV16/18 was approved having no conflicts of interest, other study investigators reported receiving financial support through royalties and employee stock options from GlaxoSmithKline, manufacturer of the vaccine used in the study—and Merck.