Cervarix Found More Immunogenic Than Gardasil

BY MIRIAM E. TUCKER

ATLANTA — The efficacy of GlaxoSmithKline's human papillomavirus vaccine against cervical intraepithelial neoplasia grade 2 or higher was confirmed in a final analysis of phase III data from more than 18,000 women in 14 countries.

And in a separate head-to-head comparison involving a total of more than 1,100 women, immune responses to the oncogenic HPV strains 16 and 18 were significantly better with GSK's Cervarix than with Merck & Co.'s HPV vaccine Gardasil, Dr. Gary Dubin said at a meeting of the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices.

GlaxoSmithKline's phase III data on Cervarix were submitted to the Food and Drug Administration in March 2009 and are still under review. The vaccine is currently licensed in more than 95 countries, said Dr. Dubin, vice president, North American clinical development, GSK.

The final analysis enrolled 18,644 women aged 15-25 years in a double-blind, randomized, controlled trial using the hepatitis A vaccine as the control. Mean follow-up was 39 months following the first of three doses.

The primary objective was to assess efficacy against the development of cervical intraepithelial neoplasia–2 (CIN2+) associated with HPV-16 and HPV-18 in women who were DNA negative and seronegative at baseline and DNA negative at 6 months for the HPV type considered in the analysis.

Among the 14,656 seronegative women who had received all three doses of study vaccine, the overall efficacy of Cervarix against HPV-16/18 CIN2+ lesions was 93%. In total, 4/7,344 Cervarix recipients and 56/7,312 controls were found to have HPV-16/18 DNA in lesions during follow-up. Irrespective of baseline serostatus, vaccine efficacy was 91% for HPV-16/18.

In the subset of 11,641 totally vaccinated naive women, defined as those who at baseline had normal cytology, had no HPV DNA for 14 oncogenic types, and were seronegative for HPV-16 and HPV-18, Cervarix efficacy was 98% against HPV-16/18 CIN2+ lesions. For the total vaccinated cohort of 18,644 women, vaccine efficacy against HPV-16/18 CIN2+ lesions was 53%, reflecting the fact that many women in this cohort had preexisting lesions, he said.

In a separate head-to-head comparison involving 1,106 women, immune responses to the oncogenic HPV strains 16 and 18 were significantly better with Cervarix than with Gardasil.

A safety analysis showed identical rates of serious adverse events (7.5% with both Cervarix and hepatitis A vaccine) and of new-onset autoimmune disease (0.8% for both).

The head-to-head comparison was the first for the two licensed vaccines using the same methodology for immunogenicity and safety.

The primary objective was to compare the geometric mean titers of HPV-16 and HPV-18 serum neutralizing antibodies at month 7 following vaccination in women aged 18-26 years. The observer-blinded study was conducted at 40 U.S. centers in a total of 1,106 women randomized to receive Cervarix or Gardasil according to the recommended administration schedules. Placebo injections were given to the Gardasil group at 1 month and the Cervarix group at 2 months.

Cervarix induced significantly higher serum neutralizing antibody titers than did Gardasil. In women aged 18-26, titers for Cervarix were 3.7-fold higher against HPV-16 and 7.3-fold higher against HPV-18 compared with results for Gardasil. In women aged 27-35 years, those differences were 4.8-fold and 9.1-fold, and for 36- to 45-year-olds, 2.3-fold and 6.8-fold.

The frequency of circulating antigen-specific memory B cells at month 7 was 2.7-fold higher with Cervarix vs. Gardasil for HPV-16 and HPV-18, and the frequency of CD4+ T-cell responses at month 7 was also significantly higher with Cervarix compared with Gardasil for both HPV-16 and HPV-18. ■