Cervarix Shows 100% Efficacy Through 5.5 Years

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ATLANTA — The investigational cervical cancer vaccine Cervarix remained 100% effective through 5.5 years in preventing cervical intraepithelial neoplasia lesions associated with human papillomavirus strains 16 and 18, Dr. Gary Dubin reported at a meeting of the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices.

The finding comes from the second interim analysis of the long-term follow-up phase of GlaxoSmithKline's primary efficacy trial for its bivalent HPV 16/18 vaccine, in which 1,113 women aged 15-25 years were randomized to receive the vaccine or placebo.

Safety, immunogenicity, and efficacy were initially evaluated for up to 27 months (Lancet 2004;365:1757-65), and the first interim analysis of the long-term follow-up phase was performed in October 2005 (Lancet 2006; 367:1247-55). The final analysis will come at the end of 2007, said Dr. Dubin, who is vice president and director of GSK's Clinical Development and Medical Affairs, Prophylactic Vaccines, North America.

No vaccine recipient had HPV 16/18–related cytology (atypical squamous cells of undetermined significance), nor cervical intraepithelial neoplasia lesions.

At 63-64 months following receipt of the first vaccine dose, ELISA titers to HPV strains 16 and 18 were both 11 times higher in the vaccine recipients than in the placebo group. From the end of the initial (27-month) study phase through a mean follow-up of 5.5 years, 1 incident HPV 16/18 infection occurred in a vaccine recipient, compared with 43 infections among the controls, giving a vaccine efficacy of 98.1%. The infection in the one vaccine recipient did not persist at 6 and 12 months, however, whereas 19 controls had persistent infection at 6 months and 9 infections persisted at 12 months.

As had been found at the two previous analyses, no vaccine recipient had HPV 16/18–related cytology classified as atypical squamous cells of undetermined significance (ASCUS) or greater, or cervical intraepithelial neoplasia(CIN) lesions. In contrast, 24 controls had HPV 16/18–related ASCUS or higher and 5 had HPV 16/18 CIN lesions at 5.5 years. Cervarix is formulated with a special adjuvant that has been shown to induce a higher and more persistent immune response, compared with vaccines formulated with aluminum salts only (Vaccine 2006;24:5937-49).

The vaccine also showed evidence of cross-protection against HPV types 45 and 31, the third and fourth most common strains associated with cervical cancer worldwide. Efficacy against incident infection with HPV 45 was 88%, and against HPV-31, 54%. Worldwide, 2.9% of all cervical cancers are attributed to HPV 31, 6.7% to HPV 45, 17.2% to HPV 18, and 53.5% to HPV 16 (Int. J. Cancer 2004; 111:278-85).

In a separate immunobridging study involving 666 women aged 15-55 years, HPV 16/18 antibody titers were of the same order of magnitude as those associated with protection in the efficacy study. There is a need for an HPV vaccine in women over 25 years of age, because new infections with HPV cancer types are estimated to occur in 5.3% of women aged 25-55 years. Moreover, although new infections do decrease with age, the risk of persistence actually increases with age. "Our target is that women over 25 years are not denied access to the GSK cervical cancer vaccine," Dr. Dubin said.

A double-blind, randomized, controlled phase III efficacy trial involving 18,665 women aged 15-25 years in 14 countries is underway. The women received either GSK's HPV vaccine or the hepatitis A vaccine as a control on a 0-, 1-, 6-month vaccination schedule. The required number of events—HPV 16/18–associated CIN2 or higher lesions—were accrued in November 2006. Those data will be presented "in the near future." A study of the vaccine's efficacy in 5,700 women over 25 years of age is also ongoing, while trials looking at coadministration with other routine adolescent vaccines, safety and immunogenicity in HIV-positive women, and other local registration trials in several countries are planned. ■