Sustained efficacy, immunogenicity, and safety for GlaxoSmithKline's HPV vaccine

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A long-term follow-up study (HPV-023; NCT00518336) shows the sustained efficacy, immunogenicity and safety of GlaxoSmithKline's human papilloma virus (HPV) vaccine Cervarix. Women vaccinated with the HPV-16/18 AS04-adjuvanted vaccine were followed for more than nine years, and vaccine efficacy (VE) against incident infection was 100%. This is the longest follow-up report for a licensed HPV vaccine.

HPV and vaccination

Persistent infection with HPV has been clearly established as the necessary cause of the overwhelming majority of cervical cancer cases. At least 40 different HPV types are known to infect the genital mucosa, of which approximately 15 are associated with cervical cancer. Among these types, HPV-16 and HPV-18 are the most common and responsible for approximately 70% of cervical cancers. Both HPV-16 and HPV-18 are included in the two licensed HPV vaccines (GSK's Cervarix and Merck's Gardasil), which are now widely available and used. Evidence of long-term efficacy against vaccine HPV-types is very important, particularly with respect to maintaining public confidence in mass vaccination programs. HPV vaccines initially were recommended for young girls and women 9-25 years of age who have not been exposed to HPV. Since HPV causes not only cervical cancer but also genital warts and anal cancer, HPV vaccines are also recommended for boys in many countries.

Previous clinical studies

An initial double-blind, randomized, multi-center vaccination study (HPV-001; NCT00689741) was started in 2001, followed for up to 27 months, and then followed by a long-term study of the entire cohort for up to 77 months (6,4 years) post initial vaccination (HPV-007; NCT00120848). HPV-007 was followed by an additional extensive study, HPV-023, results of which were recently published in the journal *Human Vaccines & Immunotherapeutics*.

HPV-023

For this study (HPV-023), participants from Brazil were invited to continue follow-up. 437 women from five centers participated in this 36-month long-term follow-up for 113 months (9.4 years). The aim of the study was to evaluate efficacy against HPV-16/18 infection and associated cyto-histopathological abnormalities, persistence of immunogenicity, and safety of the vaccine. During HPV-023, anti-HPV-16/18 antibodies were measured annually by enzyme-linked immunosorbent assay (ELISA) and pseudovirion-based neutralisation assay (PBNA). Cervical samples were tested for HPV DNA every 6 months, and cyto-pathological examinations were performed annually.

Efficacy against HPV-16/18 infections

During HPV-023, no new HPV-16/18-associated infections or cyto-histopathological abnormalities occurred in the vaccine group. In particular, VE against HPV-16/18 incident infection was 100%. VE was 95.6% against incident infection over 9.4 years. Looking at secondary endpoints, the data showed no cases of either 6- or 12-month HPV-16/18 persistent infection in the vaccine group, versus four cases and one case, respectively, in the placebo group during the 26-months follow-up.

Efficacy against cyto-histopathological abnormalities

VE against cyto-histopathological abnormalities was another secondary endpoint of the study. VE was 97.1% against atypical squamous cells of undetermined significance (ASC-US), 95% against low-grade squamous intraepithelial lesion (LISL), and 100% against cervical intraepithelial neoplasia grade 1 (CIN1+) and grade 2 (CIN2+) associated with HPV-16/18.

Immunogenicity

All vaccines remained seropositive to HPV-16/18, with antibody titers remaining several folds above natural infection levels, as measured by ELISA and PBNA. High and sustained levels of IgG antibodies were observed, reaching a plateau approximately 18 months after the first vaccine dose and remaining stable thereafter. Compared with levels following natural infection, IgG levels in the vaccine group were 10.8-fold and 10.0-fold higher for HPV-16 and HPV-18, respectively.

Confidence in mass vaccination programs

To date, these data represent the longest follow-up reported for a licensed HPV vaccine. There were no safety concerns. The study authors led by Dr Paulo S Naud from the Federal University of Rio Grande do Sul (Porto Alegre, Rio Grande do Sul, Brazil) conclude that these results should provide confidence in the duration of protection offered by HPV mass vaccination programs existing in a number of countries around the world.

Dr Ronald Ellis, Editor-in-Chief of *HV&I*, comments: "HPV vaccine has been distinctive in having achieved 100% protective efficacy in licensure trials and showing excellent persistence of protective

immunity. The data in this article show persistence of protection for about one decade, which should give adolescents and young adults an increased level of confidence in taking this vaccine and being protected against the development of cervical and other cancers."

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