

THE HUMAN PAPILLOMAVIRUS VACCINES

Genital human papillomavirus (HPV) infection is the most common sexually transmitted infection (STI) among sexually active couples. Its annual incidence is approximately 5.5 million. Overall, an estimated 75% of sexually active men and women have been exposed to HPV at some point in their lives. HPV-16 and -18 account for about 70% of cancers of the cervix, vagina and anus, and for about 30%-40% of cancers of the vulva, penis and oropharynx. Cancer of the cervix uteri is the second most cancer among women worldwide. Cancer of the penis is a rare cancer, accounting for less than 0.5% of cancers in men.

Spontaneous clearance of HPV infection is accompanied by humoral and cellular immune response against virus-specific antigens. Two vaccines, prophylactic and therapeutic ones, are considered. Prophylactic vaccines use L1 and L2 capsid proteins to induce production of conformationally-specific antibodies. They block HPV infection. Lone L1 and L2 proteins self-assemble into a capsid that is identical to the complete virion. In this way, an antibody-mediated response is induced before the body actually comes into contact with the live virion. Therapeutic vaccines are being developed to protect HPV-positive persons against tumor development. For these vaccines, researchers are targeting the activity of the E6 and E7 oncoproteines.

On June 8, 2006, the U.S. Food and Drug Administration (FDA) approved an HPV vaccine for clinical use. The HPV vaccine that has been approved is the quadrivalent vaccine that consists of recombinant viral-like particles (VLPs) of HPV 6, 11, 16, 18 mixed with an aluminum-containing adjuvant. It is manufactured by Merck & Co., Inc. and sold under the name of Gardasil®.

The new vaccine is approved for use in females 9-26 years of age. The primary target population for vaccination should be females aged 11-12 years. However, vaccination can be given to girls as young as 9 years of age. Vaccination can receive women aged 13-26 years who have been sexually active. There are still no data on the vaccine efficacy in women older than 26, and currently no data to demonstrate the efficacy of vaccination

in males; male subjects should not be vaccinated until such data become available.

The vaccine is to be administered intramuscularly either into the deltoid muscle of the arm or the high anteriolateral area of the leg. Each patient receives three 0.5 mL doses given according to the following schedule: first dose is given at the elected date, second dose two months after the first dose, and third dose six months after the first dose. According to statements from Merck, the list price of the vaccine is 120 USD *per* dose.

GlaxoSmithKline is now conducting a phase III trial of a bivalent (HPV 16, 18) vaccine, and it is going to be presented under the name of Cervarix®. Similar results to those obtained with the quadrivalent HPV vaccine have been reported with the bivalent vaccine. It is expected to be released in June next year.

Evaluation of the HPV vaccine efficiency in preventing dysplasia and cancer has been recommended as a globally accepted endpoint for population based studies.

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References

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