HPV Vaccines

Two vaccines against human papillomavirus (HPV), a sexually transmitted virus that causes cervical cancer, were approved in 2006 and 2007 after more than ten years of intensive commercial research and development. More than half of sexually active people will contract an HPV infection at some point in their lives, although only a relatively small percentage of women will develop cervical cancer.[1,2] However, this translates to an estimated 530,000 women worldwide developing cervical cancer every year and 275,000 dying from the disease.[3] The vast majority of these women—around 85 percent—live in developing countries, where life-saving services to screen for and treat precancerous lesions are unavailable (e.g., using Pap smears or other screening technologies, followed by treatment).

Both vaccines—Gardasil®, the quadrivalent vaccine, and Cervarix®, the bivalent vaccine—prevent infection and precancerous lesions caused by HPV types 16 and 18. Gardasil® also prevents infection with types 6 and 11, which cause genital warts and respiratory papillomatosis. HPV types 16 and 18 account for approximately 70 percent of cervical cancer cases worldwide. Recently, some regulatory agencies approved language stating that both vaccines also offer some degree of cross-protection against a few non-vaccine cancer-causing types. Both vaccines are given in a series of three 0.5 mL intramuscular injections over six months—Gardasil® is administered on a 0-, 2-, and 6-month schedule, and Cervarix® on a 0-, 1-, and 6-month schedule.

Efficacy, target groups for vaccination, and duration of protection

In large, international clinical trials in young adult females, both vaccines were shown to be at least 92 percent efficacious in preventing HPV infections and precancerous lesions caused by vaccine types, when administered prior to HPV infection.[4,5,6] Young adolescent girls aged 10 to 14 years are the primary target group for HPV vaccination. While efficacy against infection and lesions was not demonstrated in young adolescents (because most were not yet exposed to infection), bridging studies have shown that antibody levels after vaccination are as high or higher in the young adolescent group as in young adult females.[7,8] Some countries are also targeting a secondary group for "catch-up," often women aged 14 to 18 years. There is evidence that duration of protection is at least seven years (the length of follow-up studies published to date), and longer-term efficacy is still being evaluated.[9] The potential benefit of vaccinating boys is still under investigation, but studies to date suggest that it is not currently cost effective. For more information, see the World Health Organization (WHO) position paper on HPV vaccines, available at: www.who.int/wer/2009/wer8415.pdf.

Global use

HPV vaccines are available through the private sector in more than 100 countries, and the vaccines have been introduced into routine immunization programs in approximately 30 countries. While they are not yet widely available in the developing world, a handful of low- and middle-income countries have introduced HPV vaccines into their immunization programs, at least in limited areas, and sometimes with the help of vaccine donations.[10] Research is underway to assess the feasibility, acceptability, and cost of HPV vaccination programs in low-resource settings. For more information, visit www.path.org/projects/cervical_cancer_vaccine.php.

Manufacturers

Gardasil® is manufactured by Merck & Co., Inc. (www.merck.com). Cervarix® is manufactured by GlaxoSmithKline (www.gsk.com).

Registration status

As of January 2011, Gardasil® was licensed in 121 countries and Cervarix® in 118. However, licensed vaccines may not yet be marketed in a given country.

WHO prequalification

In 2009, WHO regulatory authorities prequalified both HPV vaccines for procurement by United Nations agencies such as the United Nations Children's Fund (UNICEF) and the Pan American Health Organization (PAHO) Revolving Fund for Vaccine Procurement.

Public-sector price agreements

The Global Alliance for Vaccines and Immunization (GAVI)—an immunization coalition of the world's top global health agencies, governments, and private partners—offers subsidized vaccines to more than 70 countries in the developing world. In late 2008, GAVI prioritized support for HPV vaccines as part of its new vaccine investment strategy, which identified the vaccines that would have the biggest impact on the disease burden in developing countries. WHO prequalification clears the way for GAVI to purchase the HPV vaccine in the future, and many low-income countries await GAVI subsidization, but this depends on GAVI raising additional donor funding.

References

1 Spitzer M. Human Papillomavirus: Epidemiology, natural history, and clinical sequelae. *OBG Management.* 2006;(Suppl 18):S5–S10.

2 Baseman JG and Koutsky LA. The epidemiology of human papillomavirus infections. *Journal of Clinical Virology* 2005;32S(2005) S16–S24.

3 Ferlay J, Shin HR, Bray F, Forman D, Mathers C and Parkin DM. GLOBOCAN 2008, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 [Internet]. Lyon, France: International Agency for Research on Cancer; 2010. Available from: http://globocan.iarc.fr Accessed January 6, 2011.

4 Paavonen J, Naud P, Salmeron J, et al. Efficacy of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine against cervical infection and precancer caused by oncogenic HPV types (PATRICIA): Final analysis of a double-blind, randomised study in young women. *The Lancet.* 2009;374(9686):301–314.

5 Schiller JT, Castellsague X, Villa LL, Hildesheim A. An update of prophylactic human papillomavirus L1 virus-like particle vaccine clinical trial results. *Vaccine.* 2008;26:K53–K61.

6 Ault KA, FUTURE II Study Group. Effect of prophylactic human papillomavirus L1 virus-like particle vaccine on risk of cervical intraepithelial neoplasia grade 2, grade 3, and adenocarcinoma in situ: A combined analysis of four randomised clinical trials. *The Lancet.* 2007;369 (9576):1861–1868.

7 Reisinger K, Block S, Lazcano-Ponce E et al. Safety and Persistent Immunogenicity of a Quadrivalent Human Papillomavirus Types 6, 11, 16, 18 L1 Virus-Like Particle Vaccine in Preadolescents and Adolescents- A Randomized Controlled Trial. Pediatr Infect Dis J 2007;26:201–209.

8 Pedersen C, Petaja T, Strauss G et al. Immunization of Early Adolescent Females with Human Papillomavirus Type 16 and 18 L1 Virus-Like Particle Vaccine Containing AS04 Adjuvant. Journal of Adolescent Health; 2007;40;564–571 Block S, Nolan T, Sattler C et al. Comparison of the Immunogenicity and Reactogenicity of a Prophylactic Quadrivalent Human Papillomavirus (Types 6, 11, 16, and 18) L1 Virus-Like Particle Vaccine in Male and Female Adolescents and Young Adult Women. Pediatrics 2006;118:2135–2145.

9 De Carvalho N, Teixeir J, Roteli-Martins CM. Sustained efficacy and immunogenicity of the HPV-16/18 AS04-adjuvanted vaccine up to 7.3 years in young adult women. *Vaccine* 2010;28: 6247–6255.

10 Wang S. Update on HPV vaccines and WHO vaccine donations policy. Presented at: Global Meeting on Implementing New and Under-utilized Vaccines. 23 June 2010; Montreux, Switzerland.

For more information on the Caucus on New and Underused RH Technologies, please visit our web page at **http://www.rhsupplies.org/working-groups/caucus-on-newunderused-rh-technologies.html.**

This publication forms part of a series of technical briefs, written by members of the Caucus on New and Underused Reproductive Health Technologies, a thematic group established under the auspices of the Reproductive Health Technologies Coalition. The Caucus' aim is to broaden the discussion within the Coalition of reproductive health technologies that are not well integrated into the public or commercial health sectors. Responsibility for the selection and contents of the product briefs rests solely with the Caucus and does not imply endorsement by the Coalition or its wider membership. For additional information, please contact **secretariat@rhsupplies.org**.

This brief was last updated January 2011.