Second HPV Vaccine Backed for Girls, Women

BY ELIZABETH MECHCATIE

SILVER SPRING, MD. — The majority of a federal advisory panel agreed that the data on a recombinant bivalent human papillomavirus vaccine indicate that the vaccine is safe and effective in preventing cervical cancer and certain precancerous or dysplastic lesions caused by HPV types 16 and 18 in girls and women aged 10-25 years.

The FDA's Vaccines and Related Biological Products Advisory Committee voted 12-1 that the data on the GlaxoSmithKline Biologicals human papillomavirus bivalent (types 16 and 18) vaccine, recombinant, supported the efficacy of the vaccine for preventing HPV 16/18–related cervical cancer, cervical intraepithelial neoplasia (CIN) 2+, adenocarcinoma in situ (AIS), and CIN1+ in girls and women aged 15-25 years.

In a separate vote, the panel again voted 12-1 that the results of an immunogenicity bridging study from the United Kingdom, which compared immune responses to the vaccine in recipients aged 10-14 years with those of older recipients, supported effectiveness of this same claim in girls aged 10-14 years. There were no efficacy data in the younger age group, but immune responses for HPV 16/18 in the younger girls were similar to those in the older group.

If approved, GSK plans to market the vaccine as Cervarix. GSK has proposed that Cervarix be licensed for prevention of cervical cancer (squamous cell cancer and adenocarcinoma) and protection against precancerous or dysplastic lesions and persistent/incident infections caused by HPV types 16 and 18, in girls and women aged 10-25 years. It is administered in a three-dose schedule at 0, 1, and 6 months.

The majority of the panel also voted that the data supported the safety of the vaccine in girls and women aged 10-25 years but recommended that safety issues, which included spontaneous abortions, be studied further after licensure. In the pivotal study, there was a higher number of spontaneous abortions around the time of vaccination than in the comparison group.

GSK, which has a Cervarix pregnancy registry in the United Kingdom, has announced plans to combine that with a U.S. registry, pending FDA approval. The company has also announced plans to conduct a postmarketing safety study.

There were more musculoskeletal and neuroinflammatory events with potential autoimmune causes—although rare—among almost 30,000 Cervarix recipients, compared with controls. The three most common adverse events associated with the vaccine were headache, injection site pain, and fever.

The FDA usually follows the recommendations of its advisory panels. HPV 16 and 18 cause most cervical cancers in the United States. The vaccine, approved in 2007 in Australia, is now licensed in 98 countries.

Merck's quadrivalent HPV vaccine, Gardasil (human papillomavirus [types 6, 11, 16, 18] quadrivalent vaccine, recombinant), is approved for girls and women aged 9-26 years, for preventing cervical, vulvar, and vaginal cancer caused by HPV types 16 and 18 as well as associated precursor lesions and genital warts caused by HPV types 6 and 11. ■

FDA Panel Supports HPV Vaccine for Boys and Men

BY ELIZABETH MECHCATIE

SILVER SPRING, MD. — In nearly unanimous votes, a Food and Drug Administration advisory panel agreed that data on Gardasil supported the efficacy and safety of the vaccine for use in preventing genital warts caused by human papillomavirus types 6 and 11 in boys and men aged 9-26 years.

At the meeting, the FDA's Vaccines and Related Biological Products Advisory Committee voted 7-0 with 1 abstention on the efficacy question and voted 7-1 on the safety question. The panel was not asked specifically on whether to recommend licensure of Gardasil (human papillomavirus [types 6, 11, 16, 18] recombinant vaccine), manufactured by Merck & Co.

The FDA usually follows the recommendations of its advisory panels. A Merck spokesperson said the company expects the FDA to make a decision during the fall. The vaccine is licensed for use in girls and women aged 9-26 years, for the prevention of cervical, vulvar, and vaginal cancer caused by the oncogenic HPV types 16 and 18, and associated precursor dysplastic lesions (CIN, VaIN, AIS), and genital warts caused by HPV 6 and 11. It has been available since 2006 and is administered in a three-dose series of intramuscular injections at 0, 2, and 6 months.

The expanded indication proposed by Merck is for use in boys and men aged 9-26 years, "for the prevention of genital warts (condyloma acuminata) caused by HPV types 6 and 11," the two HPV types that cause the majority of genital warts.

Gardasil was evaluated in a pivotal safety and efficacy study, a multinational study of approximately 4,000 boys and men aged 16-26 years, who received Gardasil or placebo; 85% were heterosexual and 15% were men having sex with men. Participants with a history of genital warts, no history of sexual activity, and those with more than five lifetime sexual partners were excluded.

The primary end point was the effect of the vaccine on the combined incidence of HPV 6/11/16/18–related external genital lesions (EGL), which included external genital warts, penile/perianal/perineal intraepithelial neoplasia (PIN), and penile, perianal, or perineal cancer.

In the approximately 1,800 subjects who received all three Gardasil doses and were tested at month 7, the vaccine was 90% effective in preventing HPV 6/11/16/18–related EGL, a highly statistically significant effect. The vaccine was 89% effective in preventing condylomata acuminata, the focus of the proposed indication. There were few cases of PIN and no cases of cancer in either placebo or Gardasil recipients.

A study of adolescent boys aged 9-15 years and of boys and men aged 16-26 years who received the three Gardasil doses determined that the immune responses to each of the four HPV types among the younger participants was not inferior to the responses seen among those in the older group.

In the pivotal trial, the number of adverse events reported within 1-15 days of any of the vaccinations was 10% higher (74% vs. 64%) among Gardasil recipients, mostly due to injection site–related adverse events (the most common was injection-site pain). Systemic adverse events were slightly more common in the vaccine group; no serious adverse events were attributed to the vaccine. More than 95% of the adverse events were mild to moderate. In the safety database of about 5,400 boys and men, no safety signals have been identified, according to the FDA. ■

Expedited Partner Treatment Said to Merit Wider Application

BY KATE JOHNSON

MONTREAL — Expedited partner treatment, also known as patient-delivered partner therapy, could substantially reduce costs and morbidity from sexually transmitted diseases if it were allowed in all states, according to Dr. Margaret Villers.

The practice allows physicians who are treating patients with sexually transmitted diseases to either provide treatment or write a prescription for their patients' partners without requiring the partners to come in to the office.

Expedited partner treatment is explicitly legal in only 19 states, and 'in multiple states and localities, there are legal barriers which may prevent universal implementation.'

Although the Centers for Disease Control and Prevention has encouraged expedited partner treatment (EPT) since 2006, it is explicitly legal in only 19 states, and "in multiple states and localities, there are legal barriers which may prevent universal implementation," Dr. Villers said at the annual meeting of the Infectious Diseases Society for Obstetrics and Gynecology. (For a map showing the legal status of EPT in each state, visit www.cdc.gov/std/ept/legal/default.htm.)

"The South Carolina statute very much mirrors the other states where it's prohibited in the sense that if you do not see a patient—if you've never met them, if you have not examined them, and if you do not have an ongoing relationship with them—then you are not allowed to prescribe a medication for them," explained Dr. Villers of the Medical University of South Carolina, Charleston.

In a cost-utility model examining the potential impact of EPT in 11 states where it was illegal in 2007 (one state, North Dakota, has since made the practice legal), she estimated there would be a cost savings of almost $6 million and the prevention of more than 2,000 cases of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* annually.

The model suggested that EPT would have resulted in 984 fewer cases of chlamydia (out of the actual 196,819 cases) and 1,280 fewer cases of gonorrhea (out of the actual 56,585 cases). This would have resulted in a net savings of $1,671,387 for chlamydia and $4,163,534 for gonorrhea, and a combined gain of 453 quality-adjusted life years, she said.

In the 19 U.S. states where EPT is explicitly legal, "there are state statutes that either allow for the provision of a prescription in general or specifically for the treatment of STDs only," she said. But the laws are "somewhat murky" in 21 states.

She said that approximately 1 year ago the American Bar Association sent an open letter to all members encouraging states and localities to pass statutes that might decrease barriers to EPT.

"Improved clarification of the legal status of EPT, whether it is a state law which only allows the prescription of medications for STDs or whether it is a broader general law, might actually make this type of treatment more acceptable to physicians," she said in an interview.

Dr. Villers noted that her study probably underestimates the benefits of EPT by assuming that the infected patient is female, and by considering only the 3-month period following her treatment. In addition, "we did not take into account multiple sexual partners, and we also only looked at direct medical costs." ■