Merck Hopes To Extend Gardasil Vaccine to Men

By Radha Chitale

Gardasil, the vaccine that protects women from common strains of the human papillomavirus (HPV) responsible for about 70% of cervical cancers, has proved successful. According to the Centers for Disease Control and Prevention’s National Immunization Survey, about 25% of women have received the vaccine. Now Merck, the pharmaceutical giant that manufactures Gardasil, is looking to match that success in men.

In a November press release, Merck announced completion of an initial study showing that Gardasil has a 90% efficacy in preventing external genital lesions caused by HPV types 6, 11, 16, and 18 in men aged 16–26 years. On the basis of this latest study as well as earlier studies in younger boys, Merck plans to seek approval from the U.S. Food and Drug Administration for Gardasil use in males aged 9–26 years to prevent external genital lesions, including genital warts, according to Tracy Ogden, a company spokesperson.

“This is the first clinical trial to demonstrate that a vaccine directed against HPV is efficacious in preventing both infection and lesions in men,” said Anna Giuliano, M.D., who led the Merck study at the H. Lee Moffitt Cancer Center in Tampa, Fla. Although the study did not produce data on whether Gardasil can protect men from penile, perineal, or anal cancers, Giuliano said that there is definitive evidence that HPV causes these cancers in men. According to the National Cancer Institute, more than 1,200 new cases of penile cancer and about 2,000 new cases of anal cancer are diagnosed in men each year in the U.S. Between 80% and 90% of anal canal cancer cases are the result of HPV—usually HPV-16—as are about 40% of all penile cancers, Giuliano said.

Moreover, because HPV is the most common sexually transmitted infection in the United States among men and women, with about 6.2 million new persons infected each year, reducing incidence of HPV in the general population could affect disease transmission as well as cancer rates.

“There’s pretty good evidence that men are a reservoir for HPV and are vectors for it,” said James Turner, M.D., professor of clinical internal medicine at the University of Virginia and chair of the Vaccine Preventable Disease Committee for the American College Health Association. “Protection makes sense, particularly if you can vaccinate boys before they become sexually active.”

If the FDA approves the vaccine for males, the CDC’s Advisory Committee on Immunization Practices (ACIP) will also review the data and recommend how the vaccine should be used. The ACIP recommendation will be important because it serves as a guideline for primary care providers. “Certainly if the ACIP recommends the HPV vaccine at age 11, it will be adopted by pediatricians and family practitioners,” Turner said. “They’ll recommend it when families come in.”

For women, the ACIP recommended that the Gardasil vaccine target girls aged 9–11 years, with catch-up vaccination recommended between ages 12 and 26 years. Merck hopes that the same will be true for males.

“The goal is for boys to be protected from something that can be prevented,” Ogden said. “And the incidence of genital lesions is high for boys.”

Marketing Challenge

If Gardasil were made available to males, the strongest push to vaccinate would probably come from family physicians and well-informed parents, according to Brigitte Miller, M.D., section head of gynecologic oncology at the Comprehensive Cancer Center of Wake Forest University in Winston-Salem, N.C. This has been true for Gardasil use in women.
But marketing Gardasil to men could prove more challenging than marketing it to women. With more than 11,000 new cases diagnosed each year in the U.S. and more than 3,000 deaths, cervical cancer is more widespread than penile or anal cancers.

Also, HPV-related cancers often occur in older men—between ages 50 and 80 years—who carry the virus for decades; in women, precancerous changes can show up on a pap test within 2–4 years of being infected and, if they are persistent and go untreated, can develop into cervical cancer when a woman is in her 30s or 40s.

“I think vaccinating adolescent males will significantly impact the transmission of the disease,” Turner said. “But it will be hard to convince… males to get the vaccine.”

However, there is already strong interest in the HPV vaccine among special populations, including college-aged men, gay men, and women older than 26 years, according to Laurie Markowitz, M.D., an epidemiologist and head of the HPV working group at the CDC. Doctors report several cases of off-label Gardasil use.

“For women it has been a simpler conversation to talk about a vaccine that can protect you against cervical cancer,” said Rachel Katzenellenbogen, M.D., assistant professor of pediatrics at the University of Washington and Seattle Children’s Hospital. “But a lot of people are excited about it [becoming available for men] and are waiting for it.”

If Gardasil receives a broad recommendation for use in males from the CDC, the uptake trajectory of the vaccine could mirror that of females, with about 25% of the population getting vaccinated. This is a typical pattern for vaccines that are not mandatory for school attendance, such as the chickenpox and the MMR (measles–mumps–rubella) vaccines. Although about 20 states have proposed legislature to mandate Gardasil vaccine use in adolescent girls, it is unclear whether it ever will be made mandatory for all school children. Mandated vaccines are typically for diseases that are equally distributed and highly communicable, something that can be spread by coughing or sneezing, for example. There are mandatory vaccines for noncommunicable diseases, such as tetanus, but those are ubiquitous and are diseases that children are susceptible to.

“This vaccine is different from the other vaccines we accept mandates for in that your risk is influenced by your behavior and is not equally distributed,” said Gail Javitt, J.D., a research scholar with the Berman Institute of Bioethics at Johns Hopkins University, Baltimore.

Research and literature on HPV has been heavily weighted toward women because they bear much of the disease burden. But now, researchers say, the field may expand. “It opens the door now to look at whether the vaccine could also prevent [infection at] other sites where we know HPV causes cancer,” Giuliano said, including oropharyngeal cancers as a result of HPV transmitted during oral sex. “The rationale to move forward now is pretty strong.”