

Gardasil Prevents Warts, HPV Infection in Males

BY MIRIAM E. TUCKER

ATLANTA — The human papillomavirus vaccine was efficacious in preventing persistent infections and genital warts caused by HPV strains 6, 11, 16, and 18 in a Merck-sponsored study of 4,065 males aged 16-26 years.

The findings were presented by Dr. Richard M. Haupt at a meeting of the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices. Merck had previously reported immunogenicity and safety data for its HPV vaccine (Gardasil) in younger males aged 9-15 years, but these are the first data on efficacy in males and the first findings in older adolescent and adult males.

The rationale for use of Gardasil in males is twofold. There is intrinsic benefit to males themselves since HPV strain 18 causes penile, anal, and oropharyngeal cancer and HPV 6 and 11 are associated with genital warts. There is also a public health benefit to vaccinating males against HPV since coverage among girls is likely to be incomplete, transition of HPV occurs efficiently between sexual partners, and "gender-neutral" vaccination would be expected to reduce overall viral transmission in the entire population, noted Dr. Haupt of Merck Research Laboratories, Whitehouse Station, N.J.

ACIP is expected to recommend the vaccine for use in males aged 11-12 at the adolescent visit, just as it is now given to girls. This should simplify implementation, Dr. Doug Campos-Outcalt, of the University of Arizona, Phoenix, said in an interview.

"There are now four vaccines recommended for adolescents. I think there will be a period of time before we get high acceptance rates, but it will help to have other vaccines being offered at the same time," said Dr. Campos-Outcalt, who serves as the liaison to



ACIP from the American Academy of Family Physicians.

In the randomized, double-blind, placebo-controlled trial, three doses of Gardasil or placebo were given at 0, 2, and 6 months. Mean follow-up for this analysis was 30 months of a planned total of 36. The study population, which came from 18 different countries, included 3,463 heterosexual males aged 16-23 years and 602 males aged 16-26 who have sex with men. Because of problems in enrollment, data collection for the latter group

Vaccine efficacy was 90.4% against external genital lesions and 85.6% in preventing infection.

DR. HAUPT

lags behind by about a year, Dr. Haupt noted. At baseline, 12% of the entire group was polymerase chain reaction-positive to at least one of the four vaccine virus types. By serology, 8% were seropositive to at least one type. With the results of PCR and serology combined, 83% of the group was naive to all four types. Moreover, most who were infected had just one type, suggesting that "the vast majority would benefit from the vaccine," Dr. Haupt said.

Per protocol, efficacy of the vaccine was 90.4% against external genital lesions, 85.6% in preventing persistent infection (from two or more consecutive visits), and 44.7% against DNA detection of a vaccine virus strain in anogenital specimen from one or more visits. All three of those results were statistically significant, he said.

Safety analysis showed similar findings to those seen in females. Local site reactions were the most common adverse event, occurring in 60% of the 2,020 Gardasil recipients and 54% of the 2,029 placebo recipients. Systemic reactions, serious adverse events, and discontinuations were uncommon and were not different between the Gardasil and placebo groups, Dr. Haupt reported.

Merck has filed an application with the Food and Drug Administration for licensure of Gardasil in males aged 9-26 years. ■

HPV Misunderstood, Feared In One Border Community

BY PATRICE WENDLING

Hispanic men and women living on the United States-Mexico border have little understanding about the human papillomavirus and its role in the etiology of cervical cancer, according to a small prospective study.

Not only were there very low levels of knowledge among these residents, but their misconceptions and confusion continued even after they were given some basic information about HPV and cervical cancer, Maria Fernandez, Ph.D., said in Carefree, Ariz., during a press conference sponsored by the American Association for Cancer Research. For example, participants tended to compare HPV with HIV and other sexually transmitted infections, and were confused or unaware that men could have HPV and transmit it.

She reported on 30 Hispanic women and 11 Hispanic men without a diagnosis of HPV who lived in Rio Grande Valley colonias (unincorporated border settlements) and participated in focus groups in Brownsville, Tex. The mean age was 41 years among the women (range, 20-74 years) and 39 years among the men (range, 19-76 years). The average annual income for a family of four in these semi-rural neighborhoods was \$13,000. About 60% of participants had not completed grade school.

Analysis of the Spanish-language focus group transcripts revealed that attitudes and concerns about HPV differed by gender, said Dr. Fernandez of the division of health promotion and behavioral sciences at the University of Texas in Houston. Women in particular viewed the disease with fatalism, interpreting a

diagnosis of HPV as a diagnosis of cancer. They expressed their fears of cancer and their belief that, once diagnosed, it is "essentially a death sentence." The women said they would be reluctant to disclose their HPV status to their partners because they believed they would be accused of infidelity. Men initially expressed anger at the possibility of an HPV diagnosis, attributing it to infidelity, Dr. Fernandez said. After a brief explanation about the ambiguity of HPV transmission, they ascribed their initial reaction to cultural ideals of machismo.

Dr. Fernandez acknowledged that the border communities and colonias face unique challenges, and that the findings of this small, qualitative study should not be generalized.

"On the other hand, it raises some interesting questions about what we've heard in many other studies about cultural norms, such as things like machismo and the way we've traditionally interpreted this concept," she said. "As we saw in these focus groups, there's sort of an initial reaction, but then people talked about standing by their partner."

Clues about these cultural norms and beliefs are essential to the design and implementation of successful and badly needed interventions for HPV prevention.

"You have to be very cautious in terms of generalizing these findings, but many of the populations that are suffering increased incidence of HPV and cervical cancer and increased mortality are in this area," Dr. Fernandez said.

The study was funded by the National Institutes of Health. The authors reported no conflicts of interest. ■

New Smallpox Vaccine Found Safer Than Existing Vaccines

BY MARY ANN MOON

The third-generation smallpox vaccine LC16m8 was found to be as immunogenic as existing smallpox vaccines but appeared to be safer in a study of over 3,000 Japanese adults.

The live, attenuated, tissue-cultured LC16m8 vaccine proved to be immunogenic in adults who had never received any smallpox vaccination, and it produced an adequate booster response in those who had been vaccinated.

As important, the LC16m8 vaccine produced minimal local reactions and no severe adverse events, said Dr. Tomoya Saito of the department of tropical medicine and parasitology, Keio University, Tokyo, and associates.

"Developing a vaccine that is safer

than first-generation vaccines yet highly immunogenic is crucial to constructing a prevention plan in the event of a bioterrorist attack," the investigators noted.

They assessed the LC16m8 vaccine in healthy personnel in the Japan Self-Defense Forces inoculated in 2002-2005. Nearly 99% were men, and all were Asian. A total of 1,529 had never been vaccinated, and 1,692 had previously been vaccinated against smallpox (JAMA 2009;301:1025-33).

The proportion of "takes"—the visible skin reactions to a single intraepidermal scarification—was comparable to that seen with other vaccines, as were serum levels of neutralizing antibodies.

The seroconversion rate was over 90% in those who were never vaccinated and 60% in those who were previ-



The lesions on this patient's arm were caused by the smallpox virus, variola major.

ously vaccinated, Dr. Saito and colleagues wrote.

There were no severe adverse events

such as autoinoculation/ contact inoculation, eczema vaccinatum, progressive vaccinia, generalized vaccinia, encephalitis, or the myopericarditis that has been "a major concern" in the U.S. vaccination program. The researchers noted that while the total sample size in the study limited their ability to "conclusively confirm that absence of severe adverse events," their results support the conclusion that LC16m8 "causes minimal local manifestations and systemic adverse effects."

The study findings suggest that LC16m8 is "a viable alternative to first-, second-, and other third-generation vaccines in a smallpox preparedness program," they added. ■

CDC/ Dr. JOHN NOBLE JR.