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Targeting HPV 16/18 shows promise in cancer risk reduction

Results from two recently released studies show that researchers are seeing progress in preventing HPV-related anal cancer and in screening for HPV-related cervical cancer.

Both sets of results were published in a recent issue of *The Lancet Oncology*.

Maurie Markman, MD, national director of medical oncology at Cancer Treatment Centers of America, said neither study represents a great leap forward, but highlights the importance of HPV as a target for prevention and treatment.

Maurie Markman, MD

In the first study, **Aimée R. Kreimer, PhD,** and colleagues recruited 4,210 Costa Rican women aged 18 to 25 years into a randomized, double blind trial to evaluate the ability of the bivalent **HPV vaccine Cervarix** (GlaxoSmithKline) to protect against persistent type-specific infection with HPV 16, HPV 18 or both, and associated precancerous lesions at the cervix. Enrollment lasted from June 28, 2004, to Dec. 21, 2005.

Participants were assigned to either Cervarix (n=2,103) or to a hepatitis A vaccine as a control (n=2,107). There were 1,989 women in a restricted cohort who were negative for cervical HPV 16 and HPV 18 DNA and negative by serology at baseline. About 71% of women in both groups provided an anal specimen. Median follow-up was roughly 48.8 months in both groups.

In the full cohort, vaccine efficacy against anal HPV 16/18 infection was 62% (95% CI, 47.1-73.1). The corresponding cervical vaccine efficacy was 76.4% (95% CI, 67-83.5).

There were 27 diagnosed HPV 16-related **anal cancers** in the vaccine group vs. 85 diagnoses in the control group, for a vaccine efficacy of 68.2% (95% CI, 51.4-79.7). For cervical cancer, researchers observed 28 diagnoses in the vaccine group compared with 116 in the control group. Vaccine efficacy against cervical HPV 16 was 75.8% (95% CI, 63.8-84.2).

For HPV 18, there were 20 diagnosed anal cancers in the vaccine group compared with 45 in the control group. Vaccine efficacy was 55.5% (95% CI, 25.2-74.2). Thirteen vaccinated patients were diagnosed with cervical cancer vs. 61 in the control group. Vaccination efficacy against cervical HPV 18 infection was 78.6% (95% CI, 62-88.7).

“This is one more little bit of evidence about the value of the vaccine,” Markman said. “This helps to say that the vaccine is as good at preventing anal cancer as preventing cervical cancer, and it is outstanding at preventing cervical cancer, but I don’t think this is a major advancement. It’s a confirmation of the tremendous value of HPV vaccination.”

He said there are 500,000 **cervical cancers** diagnosed annually worldwide and 250,000 deaths from a “completely preventable illness.”

“The vaccination is a major health care advance in providing protection against the development of

HPV, which is *the* cause of cervical cancer," Markman said. "HPV vaccination is an incredibly safe, incredibly effective, incredibly important public health advance."

ATHENA study

In the second study, a sub-analysis of the ATHENA study, researchers concluded that detection of HPV 16, HPV 18 or both provided clinical performance that was least equivalent to and more reliable than detection of atypical squamous cells of undetermined significance (ASC-US) or worse with liquid-based cytology for triage to immediate colposcopy for all HPV-positive women.

According to Markman, findings from the second study confirmed much of what was already known in the field. He said the researchers' conclusion that HPV screening could become the more cost-effective choice and would eventually replace cytology was reasonable for wealthier nations, but there should have been an explicit mention that HPV screening is more expensive.

"This is a perfectly well-done study," he said. "It is unfortunate that there was not a very specific statement acknowledging that HPV testing is more expensive than cytology."

The study was funded by Roche Molecular Systems, which manufactures the screens used in **ATHENA**.

From May 27, 2008, to Aug. 27, 2009, researchers enrolled 40,901 American women at 61 clinical centers. Eligible participants were at least 25 years old, had an intact uterus, had not received treatment for cervical intraepithelial neoplasia (CIN) within 12 months of enrollment and had valid cobas HPV and liquid-based cytology test results available.

There were 431 women diagnosed with CIN2 or worse and 274 with CIN3 or worse. Ten percent of women tested were cobas HPV-positive and 6% had abnormal cytology. Researchers obtained liquid-based cervical cytology samples from each participant and tested those samples with the first-generation Amplicor HPV test, the first-generation Linear Array HPV genotyping test and the second-generation cobas HPV test.

Colposcopy and diagnostic biopsies were done on women with ASC-US or worse cytology, those who tested positive with a first-generation HPV test and a random sample of women who tested negative for HPV and cytology.

Disease prevalence was low, with 1.1% of women diagnosed with CIN2 or worse and just 0.7% diagnosed with CIN3 or worse. Researchers said in those diagnosed with CIN3, 92% tested HPV-positive compared with 52% who had ASC-US or worse liquid-based cytology (95% CI, 33.1-47.2). Similarly, 82% of women diagnosed with CIN2 were HPV-positive vs. 48% who had ASC-US or worse liquid-based cytology.

Researchers then examined different combinations of liquid-based cytology and genotyping for HPV 16, HPV 18 or both for triage to colposcopy for women who were HPV-positive. They concluded that a positive result for HPV 16, HPV 18 or both had a sensitivity of 53.8% (95% CI, 44.9-62.5) and a positive predictive value of 10.2% (95% CI, 8.1-12.8) for CIN3 or worse in women aged 25 years or older who were HPV-positive and were negative for intraepithelial lesion or malignancy cytology. A threshold of low-grade squamous intraepithelial lesion or worse with a positive result for HPV 16, HPV 18, or both was more sensitive than detection of ASC-US or worse alone, with similar positive predictive value.

Researchers said detection of high-grade squamous intraepithelial lesion or worse in patients positive for HPV 16, HPV 18 or both had a higher sensitivity and positive predictive value compared with ASC-US or worse alone. – *by Jason Harris*

For more information:

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