HPV 16/18 Vaccine Shows Efficacy Beyond 6 Years

BY MIRIAM E. TUCKER

The human papillomavirus 16/18 vaccine showed efficacy, sustained immunogenicity, and continued safety for up to 6.4 years in a combination of initial and follow-up placebo-controlled studies involving more than 1,000 women aged 15-26 years.

The three-country, 27-site study of the human papillomavirus (HPV) vaccine Cervarix—which is now licensed in the United States, Europe, and elsewhere around the world—was funded by GlaxoSmithKline (GSK) Biologicals. It contains the HPV types 16 and 18 adjuvanted with ASO4, comprising aluminum salt and an immunostimulatory molecule that has been shown to produce higher antibody titers that are sustained over a longer period of time, compared with the same antigens adjuvanted with aluminum salts alone, according to the GSK Vaccine HPV-007 Study Group, led by Dr. Barbara Romanowski (Lancet 2009 Dec. 3 [doi:10.1016/S0140-6736(09)61567-1]).

At 6.4 years, vaccine efficacy against incident HPV-16 or HPV-18 infection in the according-to-protocol analysis involving 919 women was 95.3%.

Of 1,113 women included in the initial study, a total of 700 completed the follow-up study. The total vaccinated cohort included 560 women in the vaccine group and 553 in the placebo group, while the according-to-protocol (ATP) efficacy cohort included 465 in the vaccine group and 454 in the placebo group. At baseline, all had normal cervical cytology and were negative for both HPV-16 and -18.

The mean follow-up period from the start of the initial study was 5.9 years, with a maximum duration of 6.4 years. The study population was racially diverse and had a mean age of 20 years (range, 15-26 years) at entry to the initial study and 23 years at the beginning of follow-up.

At 6.4 years, vaccine efficacy against incident HPV-16 or HPV-18 infection in the ATP analysis was 95.3%, and long-term efficacy against persistent infection was 100% at both 6 and 12 months. said Dr. Romanowski of the University of Alberta, Edmonton, and her study group associates.

Almost all vaccine recipients (99%) remained seropositive for anti–HPV-16 and anti–HPV-18 total IgG antibodies.

In an accompanying editorial, Dr. Gary M. Clifford said that the immunogenicity data showing no evidence of further decline from 3 to 6 years are "perhaps the most interesting" because they suggest that mean antibody concentrations should remain well above those associated with natural infection long into the future.

The target age of vaccination is a balance between "being early enough to catch girls before sexual debut, but late enough to provide an as yet unknown duration of immunity that protects during as many subsequent years of sexual activity as possible," wrote Dr. Clifford of the International Agency for Research on Cancer, Lyon, France (Lancet 2009 Dec. 3 [doi:10.1016/S0140-6736(09)61789-X]). ■

Disclosures: *Dr. Clifford said that he had no conflicts of interest.*

Incontinence Symptoms Worse in Obese Women

BY DAMIAN McNAMARA

HOLLYWOOD, FLA. — Obese women planning incontinence surgery have more severe urinary incontinence symptom distress, worse quality of life, and more frequent incontinence episodes than overweight or normal-weight women, even after other obesity-related factors are controlled for, according to a secondary analysis of two large study populations.

There are limited data in the literature, however, to explain why obese women with stress urinary incontinence might experience more distress. One possibility is that increased intra-abdominal pressure in obese patients may cause chronic "stress" to the urinary bladder, leading to incontinence, Dr. Holly E. Richter said.

To find out more, Dr. Richter and her associates performed a secondary analysis of women with stress urinary incontinence seeking surgery. They assessed 655 participants from the Stress Incontinence Surgical Treatment Efficacy Trial (SISTEr) (Urology 2005;66:1213-7) and 597 patients from the ongoing Trial of Mid-Urethral Slings (TOMUS)

For the current study, the researchers pooled and grouped the women according to body mass index cutoffs for obesity (30 kg/m^2 or more), overweight (25 to less than 30 kg/m^2), and normal weight (less than 25 kg/m^2).

The Urogenital Distress Inventory (UDI) total score, incontinence episode frequency on 3-day diaries, pad weights, and Valsalva leak point pressures were higher among obese women versus overweight and normal-weight women, Dr. Richter said at the annual meeting of the American Urogynecologic Society.

Specifically, the mean UDI total score was 139 in the normal-weight women, 147 in overweight women, and 160 among obese women in SISTEr. In TOMUS, the UDI total scores were 124 in the normal-weight participants, 130 in the overweight participants, and 144 among the obese participants. The differences were statistically significant between groups in both trials.

"Obese women appear to have better urethral function," Dr. Richter said, based on their higher Valsalva leak point pressures and maximal urethral closure pressures (measured in the TOMUS study). These higher pressures might indicate a compensatory mechanism in obese women.

Other incontinence severity measures, including the UDI urge subscale score and the Incontinence Impact Questionnaire total score also were higher for obese versus other participants, said Dr. Richter, professor of obstetrics and gynecology at the University of Alabama at Birmingham.

Approximately 45% of subjects were obese in both trials. The mean age was about 52 years, the majority of women were white (75%-80%), and there was no significant difference between BMI categories in terms of diabetes incidence, Dr. Richter said.

"Obesity did not [have an] impact in terms of success of surgery, at least in the SISTEr trial," she said. ■

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HPV Cervical Ca Screening May Benefit Older Women Most

BY MICHELE G. SULLIVAN

A two-round cervical cancer screening strategy based on testing for human papillomavirus DNA may detect significantly more invasive cancers than one based on cytology.

However, the benefit could come at the expense of overtreatment, especially for younger women, Dr. Guglielmo Ronco and his colleagues reported (Lancet Onc. 2010: DOI:10.1016/S1470-2045(09)70360-2). "For young women … the detection of cervical intraepithelial neoplasia was much higher … at round one, but only slightly lower at round two, suggesting that a large number of regressive CIN2 lesions were identified and treated," wrote Dr. Ronco of the Center for Cancer Prevention, Turin, Italy, and his co-authors. "Overtreatment of regressive lesions is a problem because excisional treatment of cervical lesions is associated with increased risk of pregnancy-related morbidity."

The New Technologies for Cervical Cancer (NTCC) screening study randomized 94,000 women to one of two two-round screening programs for cervical cancer. One program was based on cytology alone and the other on HPV testing plus cytology. Women who screened positive for HPV DNA were treated according to their age. Those aged 35-60 years were referred to colposcopy, while those aged 25-34 years were referred to colposcopy only if after a year the test remained positive, or if cytology was atypical squamous cells of undetermined significance (ASCUS) or more severe.

During phase two, women were referred for colposcopy if the HPV test was positive. The primary end point was the number of women with confirmed preinvasive and invasive cervical cancers.

The subjects' median age at recruitment was 41 years. The median duration of follow-up was 3.5 years.

Both HPV and cytology detected a similar number of invasive cancers during the first round of screening (seven and nine). However, during the second round, no additional cancers were found in the HPV group, while nine cancers were found in the cytology group. Five (55%) of these were squamous cell carcinomas (one stage T1A and four stage T1B) and four (44%) were adenocarcinomas (two stage T1A, one stage T1B, and one TX). This represented a significant increase over the percentage of cervical cancers identified as adenocarcinomas by Italian cancer registries in 2005 (12%), the investigators noted.

Women aged 35-60 years reaped most of the benefit. In the first round, HPV screening detected six invasive cancers and cytology detected eight. In the second round, there were no additional cancers detected in the HPV group, and seven more identified in the cytology group.

For these women, HPV testing detected significantly more CIN2 lesions than cytology (108 vs. 54) during round 1, but significantly fewer during round 2 (8 vs. 15). For CIN3 or adenocarcinoma in situ, HPV testing detected significantly more in round 1 (98 vs. 47) and fewer in round 2 (8 vs. 17). For women aged 25-34 years, HPV testing identified 4.5 times more CIN2 lesions than did cytology testing (126 vs. 27) in round 1. In round 2, HPV testing detected significantly fewer CIN2 lesions than cytology (8 vs. 15). This suggests that the first round of screening identified many lesions that might not have needed treatment. ■

Disclosures: *The study was funded by the European Union and the Italian government. Dr. Ronco disclosed that he has been an adviser to Gen-Probe, which is developing an HPV DNA assay.*