Cervarix Is Effective Against CIN2+ Lesions

BY MIRIAM E. TUCKER

ATLANTA — The efficacy of GlaxoSmithKline’s human papillomavirus vaccine against cervical intraepithelial neoplasia grade 2 or higher has been confirmed in a final analysis of phase III data from more than 18,000 women in 14 countries.

In a separate head-to-head comparison involving a total of more than 1,100 women, immune responses to the oncogenic HPV strains 16 and 18 were significantly better with GSK’s Cervarix than with Merck & Co.’s HPV vaccine Gardasil.

Dr. Gary Dubin said at the June meeting of the Centers for Disease Control and Prevention’s Advisory Committee on Immunization Practices.

Cervarix is one of three vaccines currently licensed in more than 95 countries, according to Dr. Dubin, vice president, North American clinical development, GSK.

The final analysis enrolled 18,644 women aged 15-25 years in a double-blind, randomized, controlled trial using the hepatitis A vaccine as the control. Mean follow-up was 39 months after the first of three doses.

The primary objective was to assess efficacy against the development of cervical intraepithelial neoplasia-2 (CIN2+) associated with HPV-16 and HPV-18 in women who were DNA negative and seronegative at baseline and DNA negative at 6 months for the HPV type considered in the analysis. The final analysis was conducted when at least 36 cases of the primary end point were observed in the HPV-16/18 CIN2+ lesions was 53%, reflecting the fact that many women in this cohort had preexisting lesions, he said.

Irrespective of HPV lesion type, the efficacy of Cervarix in the naive women was 70% against CIN2+ lesions and 87% against CIN3+ lesions. For the total vaccinated cohort, irrespective of HPV lesion type, Cervarix efficacy was 30% for CIN2+ lesions and 33% for CIN3+ lesions.

Examination by the cumulative incidence over time showed that lesion development occurred at the same rate in the vaccine and control groups until about month 18, when the curve separation became apparent.

This is because most of the lesions detected during the first 18 months of the trial were derived from preexisting precursors. Only after there was a “washout” of these lesions did the prophylactic effect of the vaccine become apparent, Dr. Dubin pointed out.

Cervarix also had a significant impact on colposcopy referrals, with reductions of 26% in the naive group and 10% in the total vaccinated cohort. Cervical excision procedures were also affected, with reductions of 10% in the naive and 25% in the total vaccinated group compared with the placebo group.

Cervarix also showed efficacy against CIN2+ lesions caused by nonvaccine types that are genetically related to the vaccine types HPV-16 and HPV-18.

Severe Anemia May Not Be Obvious at AUB Presentation

BY BETSY BATES

CHICAGO — Few symptoms or clinical examination findings distinguished severely anemic patients from other women who presented for urgent evaluation of abnormal uterine bleeding, a retrospective cohort study showed.

Of 350 patients who presented to the emergency department for heavy menstrual bleeding, 122 (35%) were anemic, defined as having a hemoglobin concentration of less than 12 g/dL, while 48 (14%) were moderately to severely anemic, defined as having a hemoglobin concentration of less than 10 g/dL.

Only increasing age (relative risk, 1.04) and the presence of both tachycardia and hypertension (RR, 3.11) were associated with severe anemia, reported Dr. Kristen Matteson of the American College of Obstetricians and Gynecologists.

“Our take-home message is that clinical symptoms and bleeding history are poorly predictive for moderate to severe anemia,” said Dr. Matteson of the department of obstetrics and gynecology at Brown University, Providence, R.I.

Because no presenting symptom or physical finding can rule out clinically important anemia, she suggested that “a low threshold should be maintained for performing a hemoglobin concentration.”

The median age of women in the study was 37 years. Nearly 70% were non-Hispanic white, and 20% were non-Hispanic black. Almost one in four had received outpatient care for abnormal uterine bleeding (AUB) in the prior 3 months, but 49% had a concurrent medical condition that could affect treatment options for the condition, Dr. Matteson pointed out.

These concurrent diagnoses included breast, endometrial, or ovarian cancer; cardiovascular disease; depression; diabetes; gastrointestinal diseases; migraine; seizure disorders; and thromboembolic disorders.

The duration of the current bleeding episode was more than 7 days in 55% of the study population. A combination of heavy and irregular bleeding was reported by 65%, and more than half reported passing blood with their bleeding. Neither the amount of bleeding recorded on examination nor bleeding patterns described by the patients were associated with moderate to severe anemia.

“We were not surprised that the amount of bleeding actually seen by the provider was scant in the majority of patients because abnormal uterine bleeding can be very unpredictable and episodic,” noted Dr. Matteson. “Diagnosis and management of heavy menstrual bleeding are dependent on what a woman says about her blood loss because clinically we do not have practical means to ‘measure’ bleeding.”

When a woman reports extremely heavy bleeding that affects her life at home and work, but has little bleeding during a 30-minute medical appointment, the disparity can lead to frustration on the part of the physician and patient, she said. Studies have shown that such patients often report dissatisfaction with their interactions with health care providers.

Dr. Matteson said mild anemia is generally asymptomatic in patients who do not have cardiovascular disease. Severe anemia, on the other hand, can lead to cardiac events in some patients and may require blood transfusions. Anemia that is moderate to severe causes extreme fatigue, reducing productivity and quality of life.

Dr. Matteson reported no financial conflicts of interest.