

Addendum to the EUROGIN 2006 Programme and Abstract Book

European Research Organization on Genital Infection and Neoplasia (EUROGIN)

April 23–26, Paris, France

Additional oral presentation in

Emerging issues on HPV prophylactic vaccines - Scientific Session 15

April 26 (08:00 - 09:30) Room 342 A

Efficacy of a Prophylactic Quadrivalent Human Papillomavirus (HPV) Types 6/11/16/18 L1 Virus-Like Particle (VLP) Vaccine Through Up to 5 Years of Follow-Up

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OBJECTIVE AND METHODS: HPV can cause cervical, vulvar and vaginal cancers precancerous dysplasia and/or genital warts. A prophylactic quadrivalent HPV (type 6/11/16/18) L1 VLP vaccine (GARDASIL®, Merck & Co., Inc.) was shown to be highly effective in preventing cervical, vulvar, and vaginal cancer (via high grade dysplasia surrogates) and genital warts caused by vaccine HPV types. The risk of HPV infection is lifelong, so HPV vaccines must induce long-term protection. Here we report preliminary data for the longest term efficacy evaluation to date of an HPV vaccine.

552 16–23 year-old women were enrolled in a randomized, placebo-controlled study of quadrivalent HPV (types 6/11/16/18) L1 VLP vaccine. Subjects were not excluded from entry based on baseline HPV status. Subjects received either vaccine or placebo at Day 1, Month 2, and Month 6. At regular intervals through 3 years, subjects underwent gynecologic examination, cervicovaginal sampling for HPV DNA, serum anti-HPV testing, and Pap testing, with follow-up biopsy as indicated. A subset of 241 subjects (all subjects enrolled in Brazil and Europe) underwent 2 further years of follow-up. The primary efficacy analysis was performed in subjects who were naïve to HPV 6, 11, 16 or 18 through Month 7 (1 month Postdose 3), received all doses of vaccine/placebo, and were not protocol violators. The primary endpoint was the combined incidence of HPV 6-, 11-, 16- or 18- persistent infection or related disease, defined as HPV DNA detected in samples collected at ≥ 2 consecutive visits ≥ 4 months apart, or HPV DNA detection at the last recorded visit, or biopsies in which HPV DNA was detected and cervical, vulvar, vaginal dysplasia or genital warts was diagnosed.

RESULTS: At up to 5 years post-enrollment, the combined incidence of HPV 6-, 11-, 16- or 18-related persistent infection or disease was reduced in vaccine-recipients by 96% (95% CI: 84–100%). Of the 48 cases detected, 2 cases were in the vaccine recipients (an asymptomatic HPV 18 infection that occurred early Postdose 3 and a case of HPV 16 DNA first detected at the last recorded visit for which no further information was available). There were no cases of HPV 6-, 11-, 16-, or 18-related CIN or genital warts in vaccine recipients, and 6 cases in placebo recipients (efficacy = 100%; 95% CI: 12–100%). Vaccine induced type-specific anti-HPV geometric mean titers remained at or above those following natural infection.

DISCUSSION: We have shown a prophylactic quadrivalent HPV vaccine to be highly effective through 5 years for prevention of persistent infection, CIN and genital warts caused by HPV 6, 11, 16 or 18. This duration supports vaccination of adolescents and young adults, which is expected to greatly reduce the burden of cervical and genital cancers, precancerous dysplasia and genital warts.