Prevention is now a reality : reducing the burden of cervical cancer and other HPV disease through vaccination

MSD

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Objective : The lifetime risk of HPV infection exceeds 50%. HPV infection causes cervical cancer; a subset of vulvar and vaginal cancers; cervical, vulvar, and vaginal dysplastic lesions; and genital warts. HPV 16/18 cause 70% of cervical pre-cancers and cancers, HPV 6/11 cause 90% of genital warts, and together HPV 6/11/16/18 cause 35-50% of low grade but clinically important cervical dysplasias. A vaccine targeting these types will substantially reduce the burden of HPV disease. The following is a review of the efficacy, immunogenicity and safety of the Merck Quadrivalent HPV vaccine with updated post-licensure data.

Methods : Merck Quadrivalent HPV vaccine is the only quadrivalent HPV (Types 6/11/16/18) L1 virus-like-particle (VLP) vaccine. Efficacy trials in 20,845 16-26 year old women were conducted, with primary efficacy analyses in per-protocol populations (subjects received 3 doses; were HPV seronegative at Day 1 and HPV DNA negative through completion of vaccination). Immunogenicity studies were also conducted in 2794 boys and girls, aged 9-15 years. For all studies, serum anti-HPV levels were measured by type-specific immunoassays and summarized as anti- HPV-6, 11, 16, and 18 neutralizing antibody geometric mean titers (GMTs) and seroconversion rates. Adverse experiences were recorded (diary card).

Results : At the time of licensure, the prophylactic efficacy of a 3-dose regimen of Merck Quadrivalent HPV vaccine against HPV 16/18-related moderate/high grade cervical precancer and noninvasive cervical cancer was 100% (0 cases vaccine versus 53 cases placebo). With an additional year of follow-up, prophylactic efficacy against this endpoint was 99% (95% confidence intervals [CI]: 93%, 100%; 1 case vaccine versus 85 cases placebo), and efficacy specifically against adenocarcinoma in situ was 100% (95% CI: 31%, 100%; 0 cases vaccine versus 7 cases placebo). Updated prophylactic efficacy against HPV 6/11/16/18-related external genital lesions (vulvar/vaginal precancers and warts) was 99% (95% CI : 96%, 100%; 2 cases vaccine versus 189 cases placebo). In adult women, vaccine-induced anti-HPV responses were detected in 99.5% of subjects one month Post-dose 3. Through up to 5 years of follow-up, anti-HPV GMTs remained at or above those measured following clearance of HPV infection and efficacy was maintained. A robust immune memory was evidenced by the rapid and strong increase in GMTs triggered by the administration of an immune challenge at 4.5 years post-dose 3. In a separate study, antibodies triggered by Merck Quadrivalent HPV vaccine were found to neutralize in-vitro HPV 31 and 45 pseudovirions, pointing to a potential for protection against additional HPV types. In adolescents aged 9-15 years, Merck Quadrivalent HPV vaccine was highly immunogenic. GMTs in girls and boys were 1.7-2.7 fold higher than those observed in young adult women. In all studies, vaccine was generally well-tolerated, though a slightly higher proportion of subjects reported one or more injection site adverse experiences than the placebo group.

Conclusion : Vaccination of adolescents and young adults with Merck Quadrivalent HPV vaccine is expected to greatly reduce the burden of cervical and other genital cancers, dysplasia, and genital warts.