Efficacy of HPV vaccination in HIV infected girls

Population : HIV infected girls
Intervention: HPV vaccination
Comparison: Placebo/ no vaccination
Outcome : HPV infection

What is the scientific evidence to support administration of the currently licensed HPV vaccines to HIV (CD4+ ≥15%) infected girls to prevent cervical cancer later in life?

			Rating	Adjustment to rating
Quality Assessment	No. of studies/starting rating		2/ RCT[1] 1/ observational	4
	Factors decreasing confidence	Limitation in study design	None serious	0
		Inconsistency	None serious	0
		Indirectness	Serious[2]	-1
		Imprecision	Serious[3]	-1
		Publication bias	None serious	0
	Factors increasing confidence	Large effect	Not applicable	0
		Dose-response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			**2**
Summary of Findings	**Statement on quality of evidence**			**Our confidence in the estimate of the effect on the health outcome is limited**
	Conclusion			**Our confidence in the estimate of the effect on the health outcome is limited to support vaccination of HIV-infected young adolescent girls to prevent cervical cancer later in life.**

[1] One small RCT available as poster presentation only (*Weinberg A et al)*. This was a study of 120 North American HIV-infected girls and boys aged 7-11, some of whom were on antiretroviral therapy, vaccinated with the quadrivalent HPV vaccine. The study included a placebo group of HIV-infected children and the immune responses of HIV-infected vaccine recipients were compared with those of HIV-uninfected historic controls, most of whom were older. The report shows that the quadrivalent HPV vaccine was immunogenic- following 3 doses of the quadrivalent HPV vaccine ≥ 99.5% seroconverted to HPV types 16 and 18. However, geometric mean titres for all the four types included in the vaccine were lower for HIV-infected children than for non-HIV-infected historical controls of similar age, but differences were statistically significant only for HPV type 6 and 18. *Kahn et al* found no differences in general mean titers (GMTs) among participants taking anti-retroviral therapy (ART) vs the comparison group, but GMTs were lower in participants not taking ART vs the comparison group for HPV-16 (p = .012) and HPV-18 (p = .003). Seroconversion rates were 100% for HPV-6, -11, -16, and -18 among participants taking ART. Rates ranged from 92.3% (for HPV-18) to 100.0% (for HPV-6) among participants not taking ART. Another small RCT (*Levin et al.)* found that seroconversion to HPV types 6, 11, 16 was 100% (90% for HPV type 18) though the GMTs achieved by vaccinating HIV infected children were 30-50% lower for vaccine types 6 and 18 and around 20% lower for HPV type 11 and 16 compared to those achieved in historical controls. An 18month follow-up after the third dose from this RCT assessed HPV6, 11, 16, and 18 seropositivity to be 94%, 97%, 99%, and 76%, respectively (Weinberg et al. 2012).

[2] Weinberg A et al, Kahn et al. and Levin et al. investigated immunogenicity and did not present data on vaccine efficacy. The immunological correlates of protection are as yet unknown. Historic controls were older than HIV-infected children; other studies indicate that age influences immune response to this vaccine. Data is lacking on sustained immune response that may be a marker of long-term protection which will be essential to protect against sexually-acquired infection acquired years after vaccination. Weinberg and Levin included girls and boys in their study, Kahn included young women (16-23 years).

[3] The study included only North American children (Weinberg et al. and Levin et al.) and North American as well as Puerto Rican children (Kahn et al.), most of whom were on antiretroviral therapy which may not be representative of other HIV-infected children with more substantial immune compromise due to HIV infection or other factors or settings where ART is unavailable.

References

Levin et al. Safety and immunogenicity of a quadrivalent human papillomavirus (types 6, 11, 16, and 18) vaccine in HIV-infected children 7 to 12 years old.J Acquir Immune Defic Syndr. 2010 Oct;55(2):197-204. doi: 10.1097/QAI.0b013e3181de8d26.

Kahn et al. Immunogenicity and Safety of the Human Papillomavirus 6, 11, 16, 18 Vaccine in HIV-Infected Young Women *Clin Infect Dis. (2013) 57 (5): 735-744*

Weinberg A, et al. Safety and immunogenicity of a quadrivalent vaccine to prevent human papillomavirus (HPV) in HIV-infected children: IMPAACT P1047. Poster 619a presented at the 15th Conference on Retroviral and Opportunistic Infections, Boston, USA, February 3-6, 2008.

Weinberg A, et al. Humoral, mucosal, and cell mediated immunity against vaccine and nonvaccine genotypes after administration of quadrivalent human papillomavirus vaccine to HIV-infected children" JID 2012. Oct;206(8):1309-18.