

Efficacy of 2 vs. 3 doses of HPV vaccination in immunocompetent girls

Population : Immunocompetent females

Intervention: 2 doses of HPV vaccination in girls (9-14 years)

Comparison: 3 doses of HPV vaccination in girls or women

Outcome : Cervical Cancer

<i>What is the scientific evidence of non-inferior immunogenicity of a 2 dose HPV vaccination schedule in girls (9-14 years) compared to a three dose schedule in girls or women?</i>				
		Rating	Adjustment to rating	
Quality Assessment	No. of studies/starting rating		4/ RCT 2/ observational ⁱ	4
	Factors decreasing confidence	Limitation in study design ⁱⁱ	Serious	-1
		Inconsistency	None serious	0
		Indirectness ⁱⁱⁱ	Serious	-2
		Imprecision	None serious	0
		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			1
Summary of Findings	Statement on quality of evidence		We have very little confidence in the estimate of the effect on the health outcome.	
	Conclusion		No data vaccine efficacy against cervical cancer is available using a 2-dose HPV schedule despite non-inferior immunogenicity compared to a 3-dose HPV schedule. Evidence from 3 RCTs as well as 2 non-randomized / non-controlled trials indicate that a two dose HPV schedule in girls induces non-inferior levels of GMT to HPV 16 and 18 than a three dose schedule in girls or women. Bridging studies allow assumption of efficacy of a 2-dose vaccination schedule in girls (9-14 years).	

ⁱ 4 RCTs and two non-randomized trials (Lazcano-Ponce et al., 947 participants), (Dobson et al., 520 participants): a 2 dose schedule in girls compared to a 3 dose schedule in girls or women has proven non-inferior immunogenicity (GMTs for anti-HPV 16 and anti-HPV 18). Licensure of the three dose schedule in girls relied on the immunological bridging studies (assessment of GMT) in young women (15-25 years of age) where efficacy of this schedule has been demonstrated.

Smolen et al. based on a Phase III quadrivalent HPV vaccine RCT assessed memory T cell response which revealed that the group that received only 2 doses (Group 1) had significantly lower responses for HPV 6, 16, and 18 (P value < 0.001) compared to the 3 dose group.

ⁱⁱ Dobson et al.: allocation concealment unclear. Romanowski et al.: No information about the blinding of laboratory staff available. Sankaranarayanan et al: Study not published with limited data from abstract only. Clinical trial HPV-070 PRI (GSK): No blinding of assessor.

ⁱⁱⁱ Only immunogenicity data available, no efficacy data on protection against cervical cancer available.

Reference List

1. Clinical trial, GSK Medicine: GSK580299 Study No.: 114700(HPV-070 PRI) accessed: July 2014).
2. Dobson SR, McNeil S, Dionne M et al. Immunogenicity of 2 doses of HPV vaccine in younger adolescents vs 3 doses in young women: a randomized clinical trial. *JAMA* 2013;309(17):1793-1802.
3. Lazcano-Ponce E, Stanley M, Munoz N et al. Overcoming barriers to HPV vaccination: non-inferiority of antibody response to human papillomavirus 16/18 vaccine in adolescents vaccinated with a two-dose vs. a three-dose schedule at 21 months 3. *Vaccine* 2014;32(6):725-732.
4. Romanowski B, Schwarz TF, Ferguson LM et al. Immune response to the HPV-16/18 AS04-adjuvanted vaccine administered as a 2-dose or 3-dose schedule up to 4 years after vaccination: Results from a randomized study. *Hum Vaccin Immunother* 2014;10(5).

Romanowski B, Schwarz TF, Ferguson L, et al. Sustained immunogenicity of the HPV-16/18 AS04-adjuvanted vaccine administered as a 2-dose schedule in adolescent girls: 5-year clinical data and modelling predictions. Abstract presented at 32nd Annual Meeting of the European Society for Paediatric Infectious Diseases, Dublin, Ireland. May 6-10 2014 [internet]. http://espid.meetingxpert.net/ESPID_945/poster_94950/program.aspx (accessed June 30, 2014).
5. Sankaranarayanan R. Trial of Two versus Three Doses of Human Papillomavirus (HPV) Vaccine in India. 2013 [cited 2013 Nov 15]. 2013.
6. Smolen KK, Gelinas L, Franzen L, et al. Age of recipient and number of doses differentially impact human B and T cell immune memory responses to HPV vaccination. *Vaccine* 2012;30:3572–9.