Immunogenicity 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 : Immunogenicity (GMT)

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?				
			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	None serious	0
		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			**3**
Summary of Findings	**Statement on quality of evidence**			**We are moderately confident in the estimate of effect on health outcome. The true effect is likely to be close to the estimate of the effect.**
	Conclusion			**We are moderately confident that a 2-dose HPV schedule induces 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**

[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] 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.

		vaccination schedule in girls (9-14 years).

Reference List[1-58]

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 Societ 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.