End-of-study (Year 7) Follow-up on Efficacy and Safety of the Human Papillomavirus (HPV)-16/18 AS04-adjuvanted Vaccine Administered in Women Older than 25 Years

Maria Rowena Del Rosario-Raymundo[1*], Cosette M. Wheeler[2], S. Rachel Skinner[3], Suzanne M. Garland[4], Archana Chatterjee[5], Naveen Karkada[6], Brecht Geeraerts[7], Frank Struyf[7] on behalf of the HPV-015 VIVIANE Study Group

[1]San Pablo Colleges Medical Center, San Pablo City, Laguna, Philippines
[2]University of New Mexico, Albuquerque, NM, United States
[3]Telethon Institute for Child Health Research, Perth, WA, Sydney University Discipline of Paediatrics and Child Health, Children's Hospital Westmead, Sydney, NSW, Australia
[4]The Royal Women's Hospital and University of Melbourne, Parkville, Victoria, Australia
[5]University of South Dakota Sanford School of Medicine/Sanford Children's Specialty Clinic, Sioux Falls, South Dakota, United States
[6]GSK Pharmaceuticals India Ltd., Bangalore, India
[7]GSK Vaccines, Wavre, Belgium

Background/Objective
This study presents HPV-16/18 AS04-adjuvanted vaccine's efficacy against cervical HPV infections/associated lesions and safety up to 7 years (y) after the first vaccination of women aged >25y, in a phase III, multicentre, randomised, double-blind, placebo-controlled trial (NCT00294047, VIVIANE).

Method
Healthy women were stratified (26-35y:~45%; 36-45y:~45%; ≥46y:~10%; <15% per age stratum had prior HPV infection/treatment) and 1:1-randomised to receive 3 doses of HPV-16/18 AS04-adjuvanted vaccine or $Al(OH)_3$ at months (m) 0-1-6. Primary endpoint: vaccine efficacy (VE) against HPV-16/18-associated 6m persistent infection (PI) and/or cervical intraepithelial neoplasia grade 1 or greater (CIN1+) (in the according-to-protocol cohort for efficacy [N=4407] and total vaccinated cohort [N=5747]). Secondary endpoints: other virological (VE against 6m PI associated with HPV-16/18, with HPV-31 and HPV-45), histopathological (VE against CIN1+ associated with HPV-16/18 or irrespective of HPV type) and cytological (VE in reduction of colposcopy referrals and local cervical therapy) efficacy endpoints and safety.

Result
The table shows VE results 7y following the first vaccination. Safety profiles in both groups were similar.

Conclusion
For women older than 25 years, the HPV-16/18 AS04-adjuvanted vaccine demonstrated significant efficacy against 6m PI and/or CIN1+ associated with HPV-16/18, efficacy against CIN1+ (irrespective of HPV type), and an acceptable safety profile, 7 years post dose 1; cross-protective efficacy against 6m PI with HPV-31 and HPV-45 was also observed. Vaccine efficacy in the total vaccinated cohort appeared similar regardless of subjects' history of prior HPV infection/treatment.
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Table. Vaccine efficacy (with 96.2% confidence intervals) 7 years following the first vaccination

Endpoint	Age (years)	TVC including the 15% subset	The 15% subset*	TVC excluding the 15% subset	ATP-E
HPV-16/18-related					
6m PI and/or CIN1+	26–35	**49.9** (30.8; 64.1)	**48.6** (-11.9; 77.7)	**50.2** (28.6; 65.6)	**91.0** (74.0; 97.9)
	36–45	**64.5** (41.1; 79.4)	**71.6** (4.4; 93.8)	**62.5** (34.2; 79.5)	**89.2** (63.0; 98.1)
	≥46	**76.7** (24.7; 94.8)	**73.7** (-194.3; 99.6)	**77.3** (12.5; 96.3)	**100** (-522.6; 100)
6m PI	>25	**60.0** (46.4; 70.4)	**62.1** (21.6; 83.0)	**59.4** (44.1; 70.9)	**91.4** (79.4; 97.1)
CIN1+	>25	**44.5** (13.8; 64.8)	**60.3** (-4.5; 86.8)	**38.4** (-1.9; 63.4)	**83.7** (21.9; 98.5)
HPV-31- and HPV-45-related					
6m PI, HPV-31	>25	**29.0** (-5.4; 52.5)	-	-	**65.8** (24.9; 85.8)
6m PI, HPV-45	>25	**63.9** (38.6; 79.6)	-	-	**70.7** (34.2; 88.4)
Irrespective of HPV type					
CIN1+	>25	**22.9** (4.8; 37.7)	-	-	-
red. FCR	>25	**11.0** (-1.3; 21.8)	-	-	-
red. LCT	>25	**20.6** (-7.8; 41.7)	-	-	-

*The 15% subset, women with prior history of HPV-associated infection/treatment (only included in the TVC analysis); TVC, total vaccinated cohort, i.e. all women who received at least one vaccine dose, irrespective of their baseline HPV DNA status and serostatus; ATP-E, according-to-protocol cohort for efficacy, i.e. women HPV DNA negative at month (m) 0 and m6 and seronegative at m0 for the corresponding (if single type) or for at least one (if multiple types) HPV type; HPV, human papillomavirus; 6m PI, 6-month persistent infection; CIN1+, cervical intraepithelial neoplasia grade 1 or greater; red. FCR, reduction of first colposcopy referral; red. LCT, reduction of local cervical therapy.

Note: The results for the 15% subset and TVC excluding the 15% subset were obtained from post-hoc analyses.