Efficacy and Safety of the Human Papillomavirus (HPV)-16/18 AS04-adjuvanted Vaccine in Chinese Women: Event-triggered Analysis of a Randomized Trial

Fengcai Zhu[1], Shang-ying Hu[2], Ying Hong[3], Yuemei Hu[1], Xun Zhang[2], Yiju Zhang[1], Qinjing Pan[2], Wen-hua Zhang[2], Fang-hui Zhao[2], Chengfu Zhang[4], Xiaoping Yang[5], Jiaxi Yu[6], Jiahong Zhu[4], Yejiang Zhu[7], Feng Chen[2], Qian Zhang[2], Hong Wang[2], Changrong Wang[5], Jun Bi[6], Shiyin Xue[4], Lingling Shen[6], Yanshu Zhang[7], Yunkun He[8], Haiwen Tang[8], Naveen Karkada[9], Pemmaraju Suryakiran[9], Dan Bi[10*], Frank Struyf[10]

[1]Jiangsu Province Centre for Disease Prevention and Control, Nanjing, China [2]National Cancer Centre - Cancer Hospital - Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [3]Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China; [4]Lianshui Centre for Disease Prevention and Control, Lianshui, China; [5]Jintan Centre for Disease Prevention and Control, Jintan, China; [6]Xuzhou Centre for Disease Prevention and Control, Xuzhou, China; [7]Binhai Centre for Disease Prevention and Control, Yancheng, China; [8]GSK Vaccines, Shanghai, China; [9]GSK Pharmaceuticals India Ltd., Bangalore, India; [10]GSK Vaccines, Wavre, Belgium

Background/Objective

Cervical cancer is a major public health problem in China and the disease is commonly associated with human papillomavirus (HPV)-16 and HPV-18 genotypes [1]. A phase II/III, double-blind randomized study (NCT00779766) demonstrated that HPV-16/18 AS04-adjuvanted vaccine was highly efficacious against HPV-16/18-associated cervical infections and lesions, was immunogenic, and had an acceptable safety profile in Chinese women until approximately 4 years post-dose 1 [2]. Efficacy and safety results from an analysis triggered approximately 57 months post-dose 1 are presented here.

Method

Healthy women aged 18–25 years (N=6053) were 1:1-randomized to receive HPV-16/18 vaccine or Al(OH)3 (control) in a 3-dose schedule given at months 0-1-6. Vaccine efficacy (VE) against virological, cytological and histological endpoints associated with HPV-16/18 and other oncogenic HPV types, immunogenicity and safety were evaluated.

Result

VE against HPV-16/18-associated endpoints was demonstrated (Table). A 52.6% (95% CI: 24.5–70.9) VE against HPV-31/33/45-associated 6-month persistent infection (according-to-protocol cohort for efficacy) was shown. In the total vaccinated cohort, 50 (1.7%) and 76 (2.5%) women in the HPV-16/18 (N=3026) and control (N=3025) groups, respectively, reported serious adverse events; 2 were fatal (not vaccination-related). 8 (0.3%) and 12 (0.4%) women in the HPV-16/18 and control groups, respectively, reported new onset chronic diseases, and 2 (0.1%) women in each group reported new onset autoimmune diseases. 181 (6.0%) and 180 (6.0%) women, respectively, reported medically significant adverse events.

Conclusion

The HPV-16/18 vaccine showed high efficacy against HPV-16/18-associated virological, cytological and histological endpoints until approximately 57 months post-dose 1, and had an acceptable safety profile in Chinese women. Results were generally in line with those from studies performed in other countries [3,4]. Funding: GlaxoSmithKline Biologicals SA

Reference

1. Chen et al. Cancer Causes Control 2009;20:1705–13
2. Zhu et al. IGCS 2014; Abstract-1084
3. Lehtinen et al. Lancet Oncol 2012;13:89–99
4. Konno et al. Hum Vaccin Immunother 2014;10:1781–94

Table. Vaccine efficacy against HPV-16/18-associated virological, cytological, and histological endpoints (ATP and TVC for efficacy, seronegative and DNA-negative* women at baseline)

HPV-16/18-associated endpoint	ATP for efficacy			TVC for efficacy		
	Number of cases		Vaccine efficacy % (95% CI)	Number of cases		Vaccine efficacy % (95% CI)
	HPV-16/18 n/N	Control n/N		HPV-16/18 n/N	Control n/N	
6-month PI and/or CIN1+**	2/2524	60/2535	**96.7** (87.4–9 9.6)	5/2567	78/2587	**93.6** (84.4–98.0)
6-month PI	2/2480	54/2488	**96.3** (85.9–99.6)	4/2551	71/2571	**94.4** (84.9–98.5)
12-month PI	1/2425	32/2455	**96.9** (81.1–99.9)	3/2516	41/2536	**92.6** (76.9–98.5)
Any cytological abnormality	4/2522	53/2535	**92.4** (79.4–98.0)	6/2563	64/2585	**90.5** (78.3–96.7)
CIN1+	1/2524	15/2535	**93.2** (56.1–99.8)	2/2567	17/2587	**88.0** (49.6–98.7)
CIN2+	1/2524	8/2535	**87.3** (5.3–99.7)	1/2567	9/2587	**88.7** (18.4–99.7)

Notes: Vaccine efficacy was calculated using the conditional exact method ([1 – rate ratio] x 100) with follow-up time starting at dose 3 for the ATP for efficacy and at dose 1 for the TVC for efficacy. *For ATP for efficacy analysis, DNA-negative at months 0 and 6, for TVC for efficacy analysis, DNA-negative at month 0. **Primary objective. ATP, according-to-protocol cohort (all evaluable women who received 3 doses for whom efficacy endpoint measures were available and who had normal or low-grade cytology at baseline); TVC, total vaccinated cohort (TVC for efficacy included all women who received at least 1 dose for whom efficacy endpoint measures were available and who had normal or low-grade cytology at baseline); n, number of women reporting ≥1 event; N, number of women in each group; CI, confidence interval; PI, persistent infection; CIN1+, cervical intraepithelial neoplasia grade 1 or higher; CIN2+, cervical intraepithelial neoplasia grade 2 or higher.