The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No.: 105926 (HPV-036)

Title: A phase IIIb, double-blind, randomized, controlled study to evaluate the immunogenicity and safety of GlaxoSmithKline (GSK) Biologicals' HPV-16/18 L1 VLP AS04 vaccine administered intramuscularly, according to a 0, 1, 6 month schedule, in healthy female subjects from Malaysia aged 18 to 35 years.
HPV-16/18 L1 VLP/AS04 vaccine: GSK Biologicals' virus-like particle (VLP) vaccine against human papillomaviruses (HPV) 16/18

Rationale: This study was designed to evaluate the immunogenicity and safety of the HPV vaccine in female subjects of Malaysian origin aged 18 – 35 years.

Phase: IIIb

Study Period: 25 September 2006 to 21 December 2007.

Study Design: Double-blind, self-contained, randomized (1:1), placebo controlled study.

Centers: 2 study centers in Malaysia.

Indication: Active immunization of females to prevent persistent HPV-16 and HPV-18 infection and HPV-16 and HPV-18 associated cervical neoplasia.

Treatment: The 2 study groups were as follows:

- HPV Group received 3 doses of the HPV vaccine
- ALU Group received 3 doses of Aluminum hydroxide

Both groups received the study vaccines as an intramuscular injection in the non-dominant arm.

Objectives:

- To evaluate antibody responses against HPV-16 and HPV-18 (by enzyme-linked immunosorbent assay [ELISA]) in all HPV vaccine recipients at Month 7.

Primary Outcome/Efficacy Variable:

- Seroconversion* rates (SCR) to HPV-16 and HPV-18 as assessed by ELISA at Month 7.

* Seroconversion is defined as the appearance of anti-HPV-16 and/or anti-HPV-18 antibodies (i.e. antibody titer ≥ cut-off value) in the sera of subjects seronegative before vaccination.

Secondary Outcome/Efficacy Variable(s):

- Occurrence of serious adverse events (SAEs) throughout the study period (up to Month 7).
- Occurrence, intensity and relationship to vaccination of solicited general symptoms, and occurrence and intensity of solicited local symptoms during the 7 days (Days 0 – 6) after each and any vaccination.
- Occurrence, intensity and causal relationship to vaccination of unsolicited symptoms within 30 days (Days 0 – 29) after any vaccination.
- Occurrence of new onset chronic diseases (NOCDs) (e.g. autoimmune disorders, asthma, type I diabetes, allergies, etc.) and other medically significant conditions throughout the study period (up to Month 7) regardless of causal relationship to vaccination and intensity. Medically significant conditions were defined as: adverse events (AEs) prompting emergency room or physician visits that were not (1) related to common diseases or (2) routine visits for physical examination or vaccination, or SAEs that were not related to common diseases. Common diseases included: upper respiratory infections, sinusitis, pharyngitis, gastroenteritis, urinary tract infections, cervicovaginal yeast infections, menstrual cycle abnormalities and injury.
- Anti-HPV-16/18 antibody titers (by ELISA) at Month 0 and Month 7.

Statistical Methods:

The analyses were performed on the Total Vaccinated Cohort and the According-To-Protocol (ATP) cohort for immunogenicity.

- The Total Vaccinated Cohort included all subjects with at least one vaccine administration documented.
- The ATP cohort for analysis of immunogenicity included all evaluable subjects (i.e. those meeting all eligibility criteria, complying with the procedures defined in the protocol, with no elimination criteria during the study) for whom data concerning immunogenicity measures were available. This included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after vaccination.

Analysis of immunogenicity:

The analysis of immunogenicity was based on the ATP cohort for immunogenicity.

For each group, at each time point for which a serological result was available (Months 0 and 7) the SCR and seropositivity rates for anti-HPV-16 and anti-HPV-18 antibodies (with exact 95% confidence interval [CI]) were calculated. Geometric Mean Titers (GMTs) with 95% CI and range of antibody titers were tabulated for antibodies against each antigen.

Analysis of safety:

The analysis was performed on the Total Vaccinated Cohort.

The percentage of subjects reporting each individual solicited local and general symptom during the solicited 7-day (Days 0–6) follow-up period was tabulated with exact 95% CI. The same tabulation was performed for grade 3 symptoms and for solicited general symptoms with a causal relationship to vaccination. The percentage of subjects with at least one report of unsolicited AEs classified by the Medical Dictionary for Regulatory Activities (MedDRA) Preferred terms and reported up to 30 days (Days 0-29) after vaccination was tabulated. The same tabulation was performed for grade 3 unsolicited AEs and for unsolicited AEs with relationship to vaccination. The percentage of subjects with at least one report of an NOCD classified by MedDRA and reported during the entire study period was tabulated with exact 95% CI. The percentage of subjects with at least one report of a medically significant AE classified by MedDRA during the entire study period was also tabulated with exact 95% CI. The occurrence of SAEs was tabulated during the entire study period.

Study Population: Healthy Malaysian women aged 18 to 35 years at the time of first vaccination, with a negative urine pregnancy test before each vaccination. Subjects of childbearing potential had to be abstinent or had used adequate contraceptive precautions for 30 days prior to the first vaccination and had agreed to continue such precautions for 2 months after completion of the vaccination series. Written informed consent was obtained from each subject before entry into the study.

Number of Subjects:	**HPV Group**	**ALU Group**
Planned, N	150	150
Randomized, N (Total Vaccinated Cohort)	135	136
Completed, n (%)	131 (97.0)	135 (99.3)
Total Number Subjects Withdrawn, n (%)	4 (3.0)	1 (0.7)
Withdrawn due to Adverse Events n (%)	1 (0.7)	0 (0.0)
Withdrawn due to Lack of Efficacy n (%)	Not applicable	Not applicable
Withdrawn for other reasons n (%)	3 (2.2)	1 (0.7)
Demographics	**HPV Group**	**ALU Group**
N (Total Vaccinated Cohort)	135	136
Females:Males	135:0	136:0
Mean Age, years (SD)	24.8 (3.91)	25.0 (4.14)
Asian (South East Asian heritage), n (%)	87 (64.4)	84 (61.8)

Primary Efficacy Results: Seroconversion/seropositivity rates and GMTs for anti-HPV-16 antibodies by pre-vaccination status (ATP cohort for immunogenicity)

Group	**Pre-vaccination status**	**Timing**	**N**	**≥ 8 EL.U/mL**				**GMT (EL.U/mL)**		
				n	**%**	**95% CI**		**Value**	**95% CI**	
						LL	**UL**		**LL**	**UL**
HPV	S-	PRE	112	0	0.0	0.0	3.2	4.0	4.0	4.0
		PIII(M7)	112	112	100	96.8	100	11107.5	9727.3	12683.4
	S+	PRE	14	14	100	76.8	100	35.4	11.0	113.6
		PIII(M7)	14	14	100	76.8	100	11342.5	7240.5	17768.6
	Total	PRE	126	14	11.1	6.2	17.9	5.1	4.3	6.0
		PIII(M7)	126	126	100	97.1	100	11133.3	9817.6	12625.3
ALU	S-	PRE	117	0	0.0	0.0	3.1	4.0	4.0	4.0
		PIII(M7)	115	4	3.5	1.0	8.7	4.4	4.0	4.8
	S+	PRE	12	12	100	73.5	100	18.8	11.2	31.5
		PIII(M7)	12	7	58.3	27.7	84.8	10.6	5.4	20.8
	Total	PRE	129	12	9.3	4.9	15.7	4.6	4.2	5.0
		PIII(M7)	127	11	8.7	4.4	15.0	4.7	4.2	5.3

S- = seronegative subjects (antibody titer < 8 EL.U/mL) prior to vaccination
S+ = seropositive subjects (antibody titer ≥ 8 EL.U/mL) prior to vaccination
GMT = geometric mean antibody titer calculated on all subjects
N = number of subjects with pre-vaccination results available
n (%) = number (percentage) of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = pre-vaccination
PIII(M7) = post Dose 3, Month 7

Primary Efficacy Results: Seroconversion/seropositivity rates and GMTs for anti-HPV-18 antibodies by pre-vaccination status (ATP cohort for immunogenicity)

Group	Pre-vaccination status	Timing	N	≥ 7 EL.U/mL				GMT (EL.U/mL)		
				n	%	95% CI		Value	95% CI	
						LL	UL		LL	UL
HPV	S-	PRE	106	0	0.0	0.0	3.4	3.5	3.5	3.5
		PIII(M7)	106	106	100	96.6	100	4273.5	3771.8	4841.9
	S+	PRE	16	16	100	79.4	100	15.8	11.1	22.6
		PIII(M7)	16	16	100	79.4	100	4203.2	2578.7	6851.1
	Total	PRE	122	16	13.1	7.7	20.4	4.3	3.9	4.7
		PIII(M7)	122	122	100	97.0	100	4264.2	3771.6	4821.2
ALU	S-	PRE	113	0	0.0	0.0	3.2	3.5	3.5	3.5
		PIII(M7)	113	2	1.8	0.2	6.2	3.6	3.4	3.9
	S+	PRE	14	14	100	76.8	100	20.1	14.5	27.9
		PIII(M7)	14	12	85.7	57.2	98.2	14.6	9.1	23.2
	Total	PRE	127	14	11.0	6.2	17.8	4.2	3.8	4.7
		PIII(M7)	127	14	11.0	6.2	17.8	4.2	3.8	4.7

S- = seronegative subjects (antibody titre < 7 EL.U/mL) prior to vaccination
S+ = seropositive subjects (antibody titre ≥ 7 EL.U/mL) prior to vaccination
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with pre-vaccination results available
n (%) = number (percentage) of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = pre-vaccination
PIII(M7) = post Dose 3, Month 7

Secondary Outcome Variable(s):
Incidence of solicited local symptoms reported during the 7-day (Days 0–6) post-vaccination period after each dose and overall (Total Vaccinated Cohort)

Symptom	Intensity	HPV Group					ALU Group				
		N	n	%	95% CI		N	n	%	95% CI	
					LL	UL				LL	UL
Dose 1											
Pain	Any	132	114	86.4	79.3	91.7	135	84	62.2	53.5	70.4
	Grade 3	132	7	5.3	2.2	10.6	135	0	0.0	0.0	2.7
Redness	>0mm	132	28	21.2	14.6	29.2	135	26	19.3	13.0	26.9
	>50 mm	132	0	0.0	0.0	2.8	135	0	0.0	0.0	2.7
Swelling	>0mm	132	19	14.4	8.9	21.6	135	11	8.1	4.1	14.1
	>50 mm	132	0	0.0	0.0	2.8	135	0	0.0	0.0	2.7
Dose 2											
Pain	Any	132	90	68.2	59.5	76.0	135	56	41.5	33.1	50.3
	Grade 3	132	4	3.0	0.8	7.6	135	0	0.0	0.0	2.7
Redness	>0mm	132	28	21.2	14.6	29.2	135	10	7.4	3.6	13.2
	>50 mm	132	0	0.0	0.0	2.8	135	0	0.0	0.0	2.7
Swelling	>0mm	132	19	14.4	8.9	21.6	135	4	3.0	0.8	7.4
	>50 mm	132	1	0.8	0.0	4.1	135	0	0.0	0.0	2.7
Dose 3											
Pain	Any	130	97	74.6	66.2	81.8	133	59	44.4	35.8	53.2
	Grade 3	130	2	1.5	0.2	5.4	133	0	0.0	0.0	2.7

Redness	>0mm	130	31	23.8	16.8	32.1	133	21	15.8	10.0	23.1
	>50 mm	130	1	0.8	0.0	4.2	133	0	0.0	0.0	2.7
Swelling	>0mm	130	30	23.1	16.1	31.3	133	13	9.8	5.3	16.1
	>50 mm	130	0	0.0	0.0	2.8	133	0	0.0	0.0	2.7
Across Doses											
Pain	Any	132	121	91.7	85.6	95.8	135	101	74.8	66.6	81.9
	Grade 3	132	11	8.3	4.2	14.4	135	0	0.0	0.0	2.7
Redness	>0mm	132	48	36.4	28.2	45.2	135	40	29.6	22.1	38.1
	>50 mm	132	1	0.8	0.0	4.1	135	0	0.0	0.0	2.7
Swelling	>0mm	132	42	31.8	24.0	40.5	135	25	18.5	12.4	26.1
	>50 mm	132	1	0.8	0.0	4.1	135	0	0.0	0.0	2.7

N = number of subjects with a documented dose
n (%) = number (percentage) of subjects reporting at least once the symptom
95% CI = exact 95% confidence interval; LL = lower limit, UL = upper limit
Any = any solicited local symptom reported irrespective of intensity grade
Grade 3 pain = pain that prevented normal activity

Secondary Outcome Variable(s): Incidence of solicited general symptoms reported during the 7-day (Days 0–6) post-vaccination period following each dose and overall (Total Vaccinated Cohort)

Symptom	Intensity/ Relationship	HPV Group					ALU Group				
		N	n	%	95% CI		N	n	%	95% CI	
					LL	UL				LL	UL
Dose 1											
Arthralgia	Any	132	32	24.2	17.2	32.5	135	15	11.1	6.4	17.7
	Grade 3	132	1	0.8	0.0	4.1	135	0	0.0	0.0	2.7
	Related	132	21	15.9	10.1	23.3	135	11	8.1	4.1	14.1
Fatigue	Any	132	35	26.5	19.2	34.9	135	40	29.6	22.1	38.1
	Grade 3	132	2	1.5	0.2	5.4	135	0	0.0	0.0	2.7
	Related	132	19	14.4	8.9	21.6	135	21	15.6	9.9	22.8
Fever (Axillary)	≥37.5°C	132	5	3.8	1.2	8.6	135	6	4.4	1.6	9.4
	>39.0°C	132	1	0.8	0.0	4.1	135	0	0.0	0.0	2.7
	Related	132	3	2.3	0.5	6.5	135	2	1.5	0.2	5.2
Gastrointe-stinal symptoms	Any	132	12	9.1	4.8	15.3	135	13	9.6	5.2	15.9
	Grade 3	132	0	0.0	0.0	2.8	135	0	0.0	0.0	2.7
	Related	132	5	3.8	1.2	8.6	135	8	5.9	2.6	11.3
Headache	Any	132	32	24.2	17.2	32.5	135	38	28.1	20.8	36.5
	Grade 3	132	1	0.8	0.0	4.1	135	0	0.0	0.0	2.7
	Related	132	16	12.1	7.1	18.9	135	19	14.1	8.7	21.1
Myalgia	Any	132	38	28.8	21.2	37.3	135	27	20.0	13.6	27.7
	Grade 3	132	0	0.0	0.0	2.8	135	0	0.0	0.0	2.7
	Related	132	33	25.0	17.9	33.3	135	20	14.8	9.3	21.9
Rash	Any	132	2	1.5	0.2	5.4	135	5	3.7	1.2	8.4
	Grade 3	132	0	0.0	0.0	2.8	135	0	0.0	0.0	2.7
	Related	132	1	0.8	0.0	4.1	135	3	2.2	0.5	6.4
Urticaria	Any	132	1	0.8	0.0	4.1	135	2	1.5	0.2	5.2
	Grade 3	132	1	0.8	0.0	4.1	135	0	0.0	0.0	2.7
	Related	132	1	0.8	0.0	4.1	135	0	0.0	0.0	2.7
Dose 2											
Arthralgia	Any	132	19	14.4	8.9	21.6	135	9	6.7	3.1	12.3
	Grade 3	132	1	0.8	0.0	4.1	135	0	0.0	0.0	2.7
	Related	132	15	11.4	6.5	18.0	135	5	3.7	1.2	8.4
Fatigue	Any	132	23	17.4	11.4	25.0	135	18	13.3	8.1	20.3
	Grade 3	132	1	0.8	0.0	4.1	135	0	0.0	0.0	2.7
	Related	132	14	10.6	5.9	17.2	135	9	6.7	3.1	12.3
Fever (Axillary)	≥37.5°C	132	9	6.8	3.2	12.5	135	4	3.0	0.8	7.4
	>39.0°C	132	0	0.0	0.0	2.8	135	0	0.0	0.0	2.7

	Related	132	5	3.8	1.2	8.6	135	2	1.5	0.2	5.2
Gastrointe-stinal symptoms	Any	132	5	3.8	1.2	8.6	135	2	1.5	0.2	5.2
	Grade 3	132	0	0.0	0.0	2.8	135	0	0.0	0.0	2.7
	Related	132	3	2.3	0.5	6.5	135	1	0.7	0.0	4.1
Headache	Any	132	17	12.9	7.7	19.8	135	16	11.9	6.9	18.5
	Grade 3	132	0	0.0	0.0	2.8	135	0	0.0	0.0	2.7
	Related	132	10	7.6	3.7	13.5	135	7	5.2	2.1	10.4
Myalgia	Any	132	21	15.9	10.1	23.3	135	12	8.9	4.7	15.0
	Grade 3	132	1	0.8	0.0	4.1	135	0	0.0	0.0	2.7
	Related	132	19	14.4	8.9	21.6	135	10	7.4	3.6	13.2
Rash	Any	132	2	1.5	0.2	5.4	135	1	0.7	0.0	4.1
	Grade 3	132	0	0.0	0.0	2.8	135	0	0.0	0.0	2.7
	Related	132	1	0.8	0.0	4.1	135	0	0.0	0.0	2.7
Urticaria	Any	132	2	1.5	0.2	5.4	135	0	0.0	0.0	2.7
	Grade 3	132	0	0.0	0.0	2.8	135	0	0.0	0.0	2.7
	Related	132	1	0.8	0.0	4.1	135	0	0.0	0.0	2.7
Dose 3											
Arthralgia	Any	130	15	11.5	6.6	18.3	133	12	9.0	4.7	15.2
	Grade 3	130	1	0.8	0.0	4.2	133	0	0.0	0.0	2.7
	Related	130	12	9.2	4.9	15.6	133	8	6.0	2.6	11.5
Fatigue	Any	130	26	20.0	13.5	27.9	133	16	12.0	7.0	18.8
	Grade 3	130	1	0.8	0.0	4.2	133	0	0.0	0.0	2.7
	Related	130	14	10.8	6.0	17.4	133	12	9.0	4.7	15.2
Fever (Axillary)	≥37.5°C	130	8	6.2	2.7	11.8	133	7	5.3	2.1	10.5
	>39.0°C	130	0	0.0	0.0	2.8	133	0	0.0	0.0	2.7
	Related	130	5	3.8	1.3	8.7	133	5	3.8	1.2	8.6
Gastrointe-stinal symptoms	Any	130	3	2.3	0.5	6.6	133	4	3.0	0.8	7.5
	Grade 3	130	1	0.8	0.0	4.2	133	1	0.8	0.0	4.1
	Related	130	2	1.5	0.2	5.4	133	3	2.3	0.5	6.5
Headache	Any	130	16	12.3	7.2	19.2	133	10	7.5	3.7	13.4
	Grade 3	130	2	1.5	0.2	5.4	133	0	0.0	0.0	2.7
	Related	130	12	9.2	4.9	15.6	133	8	6.0	2.6	11.5
Myalgia	Any	130	29	22.3	15.5	30.4	133	13	9.8	5.3	16.1
	Grade 3	130	1	0.8	0.0	4.2	133	0	0.0	0.0	2.7
	Related	130	25	19.2	12.8	27.1	133	11	8.3	4.2	14.3
Rash	Any	130	1	0.8	0.0	4.2	133	1	0.8	0.0	4.1
	Grade 3	130	0	0.0	0.0	2.8	133	0	0.0	0.0	2.7
	Related	130	1	0.8	0.0	4.2	133	1	0.8	0.0	4.1
Urticaria	Any	130	1	0.8	0.0	4.2	133	0	0.0	0.0	2.7
	Grade 3	130	0	0.0	0.0	2.8	133	0	0.0	0.0	2.7
	Related	130	0	0.0	0.0	2.8	133	0	0.0	0.0	2.7
Across doses											
Arthralgia	Any	132	39	29.5	21.9	38.1	135	26	19.3	13.0	26.9
	Grade 3	132	2	1.5	0.2	5.4	135	0	0.0	0.0	2.7
	Related	132	27	20.5	13.9	28.3	135	18	13.3	8.1	20.3
Fatigue	Any	132	52	39.4	31.0	48.3	135	48	35.6	27.5	44.2
	Grade 3	132	3	2.3	0.5	6.5	135	0	0.0	0.0	2.7
	Related	132	29	22.0	15.2	30.0	135	27	20.0	13.6	27.7
Fever (Axillary)	≥37.5 °C	132	19	14.4	8.9	21.6	135	17	12.6	7.5	19.4
	>39.0 °C	132	1	0.8	0.0	4.1	135	0	0.0	0.0	2.7
	Related	132	12	9.1	4.8	15.3	135	9	6.7	3.1	12.3
Gastrointe-stinal symptoms	Any	132	18	13.6	8.3	20.7	135	18	13.3	8.1	20.3
	Grade 3	132	1	0.8	0.0	4.1	135	1	0.7	0.0	4.1
	Related	132	9	6.8	3.2	12.5	135	11	8.1	4.1	14.1
Headache	Any	132	46	34.8	26.8	43.6	135	47	34.8	26.8	43.5

	Grade 3	132	3	2.3	0.5	6.5	135	0	0.0	0.0	2.7
	Related	132	27	20.5	13.9	28.3	135	25	18.5	12.4	26.1
Myalgia	Any	132	48	36.4	28.2	45.2	135	32	23.7	16.8	31.8
	Grade 3	132	2	1.5	0.2	5.4	135	0	0.0	0.0	2.7
	Related	132	39	29.5	21.9	38.1	135	23	17.0	11.1	24.5
Rash	Any	132	4	3.0	0.8	7.6	135	7	5.2	2.1	10.4
	Grade 3	132	0	0.0	0.0	2.8	135	0	0.0	0.0	2.7
	Related	132	3	2.3	0.5	6.5	135	4	3.0	0.8	7.4
Urticaria	Any	132	4	3.0	0.8	7.6	135	2	1.5	0.2	5.2
	Grade 3	132	1	0.8	0.0	4.1	135	0	0.0	0.0	2.7
	Related	132	2	1.5	0.2	5.4	135	0	0.0	0.0	2.7

N = number of subjects with a documented dose
n (%) = number (percentage) of subjects reporting at least once the symptom
95% CI = exact 95% confidence interval; LL = lower limit, UL = upper limit
Any = any solicited general symptom reported irrespective of intensity grade and relationship to vaccination
Related = symptoms considered by the investigator to have a causal relationship to vaccination
Grade 3 Arthralgia/ Fatigue/ Gastrointestinal symptoms/ Headache/ Myalgia/ Rash = prevented normal activity
Grade 3 Urticaria = urticaria distributed on at least 4 body areas

Secondary Outcome Variable(s): Percentage of subjects with NOCDs reported during the entire study period (Day 0 up to Month 7) (Total Vaccinated Cohort)

New onset chronic diseases	**HPV Group N = 135**				**ALU Group N = 136**			
			95% CI				**95% CI**	
	n	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Subjects with any NOCD	1	0.7	0.0	4.1	0	0.0	0.0	2.7
Rhinitis allergic	1	0.7	0.0	4.1	0	0.0	0.0	2.7

At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with a documented dose
n (%) = number (percentage) of subjects reporting at least once the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable(s) - Percentage of subjects with medically significant AEs reported during the entire study period (Day 0 up to Month 7) (Total Vaccinated Cohort)

Medically significant AEs	**HPV N = 135**				**ALU N = 136**			
			95% CI				**95% CI**	
	n	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom	10	7.4	3.6	13.2	11	8.1	4.1	14.0
Keratitis	1	0.7	0.0	4.1	0	0.0	0.0	2.7
Pyrexia	0	0.0	0.0	2.7	1	0.7	0.0	4.0
Cholelithiasis	1	0.7	0.0	4.1	0	0.0	0.0	2.7
Dengue fever	1	0.7	0.0	4.1	1	0.7	0.0	4.0
Influenza	1	0.7	0.0	4.1	4	2.9	0.8	7.4
Measles	0	0.0	0.0	2.7	1	0.7	0.0	4.0
Pyoderma	1	0.7	0.0	4.1	0	0.0	0.0	2.7
Varicella	0	0.0	0.0	2.7	1	0.7	0.0	4.0
Overdose	0	0.0	0.0	2.7	1	0.7	0.0	4.0
Intervertebral disc protrusion	0	0.0	0.0	2.7	1	0.7	0.0	4.0
Dizziness	1	0.7	0.0	4.1	1	0.7	0.0	4.0
Migraine	1	0.7	0.0	4.1	0	0.0	0.0	2.7
Abortion missed	1	0.7	0.0	4.1	0	0.0	0.0	2.7
Cough	1	0.7	0.0	4.1	0	0.0	0.0	2.7
Nasal turbinate hypertrophy	1	0.7	0.0	4.1	0	0.0	0.0	2.7
Rash macular	1	0.7	0.0	4.1	0	0.0	0.0	2.7
Rash papular	1	0.7	0.0	4.1	0	0.0	0.0	2.7

At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with a documented dose

n (%) = number (percentage) of subjects reporting at least once the symptom 95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit		
Safety results: Number (%) of subjects with unsolicited AEs (Total Vaccinated Cohort)		
Most frequent adverse events - On-Therapy (occurring within Day 0-29 following vaccination)	**HPV Group N = 135**	**ALU Group N = 136**
Subjects with any AE(s), n (%)	30 (22.2)	36 (26.5)
Subjects with any Grade 3 AE(s), n (%)	2 (1.5)	4 (2.9)
Subjects with related AE(s), n (%)	11 (8.1)	11 (8.1)
Upper respiratory tract infection	8 (5.9)	10 (7.4)
Influenza	3 (2.2)	8 (5.9)
Headache	3 (2.2)	2 (1.5)
Pyrexia	2 (1.5)	3 (2.2)
Dysmenorrhea	2 (1.5)	2 (1.5)
Pharyngolaryngeal pain	1 (0.7)	3 (2.2)
Rhinorrhea	2 (1.5)	2 (1.5)
Migraine	1 (0.7)	2 (1.5)
Dengue fever	1 (0.7)	1 (0.7)
Dizziness	1 (0.7)	1 (0.7)
Nasopharyngitis	1 (0.7)	1 (0.7)
Pruritus	1 (0.7)	1 (0.7)
Back pain	-	1 (0.7)
Cough	1 (0.7)	-
Diarrhea	-	1 (0.7)
Ear pain	-	1 (0.7)
Eye irritation	-	1 (0.7)
Gingival bleeding	1 (0.7)	-
Keratitis	1 (0.7)	-
Measles	-	1 (0.7)
Menorrhagia	-	1 (0.7)
Metrorrhagia	-	1 (0.7)
Overdose	-	1 (0.7)
Pain	1 (0.7)	-
Pruritus generalized	-	1 (0.7)
Pyoderma	1 (0.7)	-
Rash macular	1 (0.7)	-
Rash papular	1 (0.7)	-
Rhinitis allergic	1 (0.7)	-
Sinusitis	1 (0.7)	-
Temperature intolerance	1 (0.7)	-
Throat irritation	1 (0.7)	-
Tonsillitis	-	1 (0.7)
Vulvovaginal burning sensation	1 (0.7)	-
- : Adverse event absent Grade 3: event that prevented normal activities Related: event considered by the investigator to be causally related to the study vaccination.		
Safety Results: Number (%) of subjects with SAEs reported during the entire study period (Day 0 up to Month 7) for the Total Vaccinated Cohort		
Serious adverse event, n (%)[n considered by the investigator to be related to study medication]		
All SAEs	**HPV Group N = 135**	**ALU Group N = 136**
Subjects with any SAE(s), n (%) [n related]	3 (2.2) [0]	3 (2.2) [0]
Dengue fever	1 (0.7) [0]	1 (0.7) [0]
Abortion missed	1 (0.7) [0]	0 (0.0) [0]
Cholelithiasis	1 (0.7) [0]	0 (0.0) [0]
Chronic tonsillitis	1 (0.7) [0]	0 (0.0) [0]

Intervertebral disc protrusion	0 (0.0) [0]	1 (0.7) [0]
Nasal turbinate hypertrophy	1 (0.7) [0]	0 (0.0) [0]
Overdose	0 (0.0) [0]	1 (0.7) [0]
Fatal SAEs	**HPV Group N = 135**	**ALU Group N = 136**
Subjects with fatal SAE(s), n (%) [n related]	0 (0.0) [0]	0 (0.0) [0]

Conclusion: One month after the third dose of the HPV vaccine (Month 7), all subjects in the HPV Group had anti-HPV-16 antibody titers ≥ 8 EL.U/mL and anti-HPV-18 antibody titers ≥ 7 EL.U/mL. Solicited local symptoms were reported more frequently in the HPV Group than in the ALU Group. Reporting rates of solicited general symptoms were similar in both groups, except for myalgia and arthralgia that were reported with a higher incidence in the HPV Group than in the ALU Group. During the 30-day follow-up period after vaccination, at least one unsolicited AE was reported by 30 (22.2%) subjects in the HPV Group and by 36 (26.5%) subjects in the ALU Group. During the entire study period, 1 NOCD was reported for 1 subject in the HPV Group; 10 (7.4%) subjects from HPV Group and 11 (8.1%) subjects from ALU Group reported a medically significant AE; SAEs were reported by 6 subjects (3 subjects in each group). None of the SAEs were considered by the investigators to have a causal relationship to vaccination. There were no fatal events reported throughout the study period.
Please also refer to the publication below.

Publications:
Verstraeten T et al. (2008) Analysis of adverse events of potential autoimmune aetiology in a large integrated safety database of AS04 adjuvanted vaccines. Vaccine. 26(51):6630–6638.

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