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.: 107291 (HPV-038)

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 aged 15 – 25 years.
HPV-16/18 L1 VLP AS04 vaccine: GSK Biologicals' virus-like particle (VLP) vaccine against human papillomaviruses 16/18 (HPV).

Rationale: This study was designed to evaluate the immunogenicity and safety of the HPV vaccine in female subjects aged 15 – 25 years in Korea.

Phase: IIIb.

Study Period: 11 June 2007 to 31 March 2008.

Study Design: Double-blind, self-contained, randomized (2:1), placebo controlled study with 2 parallel groups.

Centers: 6 study centers in Korea.

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 Aluminium hydroxide

The study vaccines were administered 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.
- Anti-HPV-16/18 antibody titers (by ELISA) at Month 0 and Month 7.
- The occurrence of new onset chronic diseases (e.g. autoimmune disorders, asthma, type I diabetes, allergies etc.) and other medically significant conditions in all groups 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.
- Occurrence of pregnancies and pregnancy outcomes throughout the study period (up to 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 vaccinated subjects for whom data were available.
- 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 endpoint 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 performed 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 following were calculated:
SCR and seropositivity rates for anti-HPV-16 and anti-HPV-18 antibodies with exact 95% confidence interval (CI)
Geometric Mean Titers (GMTs) with 95% CI and range of antibody titers were tabulated for antibodies for each antigen.

Analysis of safety:
The analysis of safety 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 AEs and for solicited general AEs 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 Term and reported during 30 days (Days 0-29) follow-up period after vaccination was tabulated. The same tabulation was performed for grade 3 unsolicited AEs and for unsolicited AEs causally related to vaccination. The percentage of subjects with at least one report of an NOCD and a medically significant classified by MedDRA and reported during the entire study period was tabulated. The occurrence of SAEs, the pregnancies and pregnancy outcomes were tabulated during the entire study period.

Study Population: Healthy Korean females aged 15 to 25 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 to use adequate contraceptive precautions for 30 days prior to 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 as well as from the parent/guardian of each subject below legal age, prior to the performance of any study-specific procedures.

Number of Subjects:	**HPV Group**	**ALU Group**
Planned, N	150	75
Randomized, N (Total Vaccinated Cohort)	149	76
Completed, n (%)	141 (94.6)	67 (88.2)
Total Number Subjects Withdrawn, n (%)	8 (5.4)	9 (11.8)
Withdrawn due to Adverse Events n (%)	0 (0.0)	0 (0.0)
Withdrawn due to Lack of Efficacy n (%)	Not applicable	
Withdrawn for other reasons n (%)	8 (5.4)	9 (11.8)
Demographics	**HPV Group**	**ALU Group**
N (Total Vaccinated Cohort)	149	76
Females: Males	149:0	76:0
Mean Age, years (SD)	22.0 (2.24)	21.9 (2.63)
Asian (East-Asian heritage), n (%)	149 (100)	76 (100)

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	125	0	0.0	0.0	2.9	4.0	4.0	4.0
		PIII(M7)	125	125	100	97.1	100	9351.4	8145.5	10735.8
	S+	PRE	11	11	100	71.5	100	23.0	12.2	43.3
		PIII(M7)	11	11	100	71.5	100	7918.1	4683.5	13386.7
	Total	PRE	136	11	8.1	4.1	14.0	4.6	4.2	5.1
		PIII(M7)	136	136	100	97.3	100	9226.4	8085.4	10528.4
ALU	S-	PRE	61	0	0.0	0.0	5.9	4.0	4.0	4.0
		PIII(M7)	61	2	3.3	0.4	11.3	4.1	3.9	4.3
	S+	PRE	6	6	100	54.1	100	33.2	14.9	73.8
		PIII(M7)	6	5	83.3	35.9	99.6	28.8	9.2	89.6
	Total	PRE	67	6	9.0	3.4	18.5	4.8	4.1	5.7
		PIII(M7)	67	7	10.4	4.3	20.3	4.9	4.2	5.8

S- = seronegative subjects (antibody titer < 8 EL.U/mL) prior to vaccination
S+ = seropositive subjects (antibody titer ≥ 8 EL.U/mL) prior to vaccination
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	122	0	0.0	0.0	3.0	3.5	3.5	3.5
		PIII(M7)	122	122	100	97.0	100	4204.1	3626.5	4873.6
	S+	PRE	13	13	100	75.3	100	16.3	9.5	27.8
		PIII(M7)	13	13	100	75.3	100	4595.0	2970.2	7108.5
	Total	PRE	135	13	9.6	5.2	15.9	4.1	3.7	4.4
		PIII(M7)	135	135	100	97.3	100	4240.2	3692.1	4869.7
ALU	S-	PRE	61	0	0.0	0.0	5.9	3.5	3.5	3.5
		PIII(M7)	60	3	5.0	1.0	13.9	3.8	3.4	4.3
	S+	PRE	6	6	100	54.1	100	15.6	5.6	43.1
		PIII(M7)	6	5	83.3	35.9	99.6	14.1	5.1	38.6
	Total	PRE	67	6	9.0	3.4	18.5	4.0	3.5	4.5
		PIII(M7)	66	8	12.1	5.4	22.5	4.3	3.7	5.0

S- = seronegative subjects (antibody titer < 7 EL.U/mL) prior to vaccination
S+ = seropositive subjects (antibody titer ≥ 7 EL.U/mL) prior to vaccination
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 across doses (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	145	136	93.8	88.5	97.1	72	51	70.8	58.9	81.0
	Grade 3	145	8	5.5	2.4	10.6	72	1	1.4	0.0	7.5
Redness	Any	145	78	53.8	45.3	62.1	72	28	38.9	27.6	51.1
	> 50 mm	145	2	1.4	0.2	4.9	72	1	1.4	0.0	7.5
Swelling	Any	145	52	35.9	28.1	44.2	72	11	15.3	7.9	25.7
	> 50 mm	145	2	1.4	0.2	4.9	72	0	0.0	0.0	5.0
Dose 2											
Pain	Any	143	126	88.1	81.6	92.9	71	45	63.4	51.1	74.5
	Grade 3	143	3	2.1	0.4	6.0	71	0	0.0	0.0	5.1
Redness	Any	143	79	55.2	46.7	63.6	71	16	22.5	13.5	34.0
	> 50 mm	143	2	1.4	0.2	5.0	71	0	0.0	0.0	5.1
Swelling	Any	143	56	39.2	31.1	47.7	71	5	7.0	2.3	15.7
	> 50 mm	143	2	1.4	0.2	5.0	71	0	0.0	0.0	5.1
Dose 3											
Pain	Any	141	119	84.4	77.3	90.0	67	43	64.2	51.5	75.5
	Grade 3	141	8	5.7	2.5	10.9	67	0	0.0	0.0	5.4
Redness	Any	141	82	58.2	49.6	66.4	67	19	28.4	18.0	40.7
	> 50 mm	141	0	0.0	0.0	2.6	67	0	0.0	0.0	5.4

Swelling	Any	141	63	44.7	36.3	53.3	67	9	13.4	6.3	24.0
	> 50 mm	141	1	0.7	0.0	3.9	67	0	0.0	0.0	5.4
Across Doses											
Pain	Any	145	140	96.6	92.1	98.9	72	64	88.9	79.3	95.1
	Grade 3	145	17	11.7	7.0	18.1	72	1	1.4	0.0	7.5
Redness	Any	145	109	75.2	67.3	82.0	72	35	48.6	36.7	60.7
	> 50 mm	145	4	2.8	0.8	6.9	72	1	1.4	0.0	7.5
Swelling	Any	145	89	61.4	52.9	69.3	72	19	26.4	16.7	38.1
	> 50 mm	145	5	3.4	1.1	7.9	72	0	0.0	0.0	5.0

N = number of subjects with at least one 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 (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	145	21	14.5	9.2	21.3	72	4	5.6	1.5	13.6
	Grade 3	145	2	1.4	0.2	4.9	72	0	0.0	0.0	5.0
	Related	145	6	4.1	1.5	8.8	72	1	1.4	0.0	7.5
Fatigue	Any	145	73	50.3	41.9	58.7	72	28	38.9	27.6	51.1
	Grade 3	145	5	3.4	1.1	7.9	72	0	0.0	0.0	5.0
	Related	145	23	15.9	10.3	22.8	72	10	13.9	6.9	24.1
Fever (Axillary)	≥37.5°C	145	2	1.4	0.2	4.9	72	1	1.4	0.0	7.5
	>39.0°C	145	0	0.0	0.0	2.5	72	0	0.0	0.0	5.0
	Related	145	1	0.7	0.0	3.8	72	0	0.0	0.0	5.0
Gastrointestinal symptoms	Any	145	30	20.7	14.4	28.2	72	12	16.7	8.9	27.3
	Grade 3	145	0	0.0	0.0	2.5	72	0	0.0	0.0	5.0
	Related	145	13	9.0	4.9	14.8	72	1	1.4	0.0	7.5
Headache	Any	145	46	31.7	24.3	40.0	72	24	33.3	22.7	45.4
	Grade 3	145	2	1.4	0.2	4.9	72	2	2.8	0.3	9.7
	Related	145	14	9.7	5.4	15.7	72	7	9.7	4.0	19.0
Myalgia	Any	145	76	52.4	44.0	60.8	72	27	37.5	26.4	49.7
	Grade 3	145	1	0.7	0.0	3.8	72	1	1.4	0.0	7.5
	Related	145	39	26.9	19.9	34.9	72	16	22.2	13.3	33.6
Rash	Any	145	17	11.7	7.0	18.1	72	5	6.9	2.3	15.5
	Grade 3	145	0	0.0	0.0	2.5	72	0	0.0	0.0	5.0
	Related	145	6	4.1	1.5	8.8	72	0	0.0	0.0	5.0
Urticaria	Any	145	6	4.1	1.5	8.8	72	2	2.8	0.3	9.7
	Grade 3	145	1	0.7	0.0	3.8	72	0	0.0	0.0	5.0
	Related	145	2	1.4	0.2	4.9	72	0	0.0	0.0	5.0
Dose 2											
Arthralgia	Any	143	11	7.7	3.9	13.3	71	2	2.8	0.3	9.8
	Grade 3	143	0	0.0	0.0	2.5	71	0	0.0	0.0	5.1
	Related	143	1	0.7	0.0	3.8	71	1	1.4	0.0	7.6
Fatigue	Any	143	69	48.3	39.8	56.8	71	26	36.6	25.5	48.9
	Grade 3	143	4	2.8	0.8	7.0	71	0	0.0	0.0	5.1
	Related	143	26	18.2	12.2	25.5	71	11	15.5	8.0	26.0
Fever (Axillary)	≥37.5°C	143	3	2.1	0.4	6.0	71	0	0.0	0.0	5.1
	>39.0°C	143	0	0.0	0.0	2.5	71	0	0.0	0.0	5.1
	Related	143	0	0.0	0.0	2.5	71	0	0.0	0.0	5.1
Gastrointestinal	Any	143	22	15.4	9.9	22.4	71	3	4.2	0.9	11.9

symptoms	Grade 3	143	1	0.7	0.0	3.8	71	0	0.0	0.0	5.1
	Related	143	7	4.9	2.0	9.8	71	0	0.0	0.0	5.1
Headache	Any	143	41	28.7	21.4	36.8	71	11	15.5	8.0	26.0
	Grade 3	143	1	0.7	0.0	3.8	71	1	1.4	0.0	7.6
	Related	143	16	11.2	6.5	17.5	71	6	8.5	3.2	17.5
Myalgia	Any	143	58	40.6	32.4	49.1	71	15	21.1	12.3	32.4
	Grade 3	143	1	0.7	0.0	3.8	71	1	1.4	0.0	7.6
	Related	143	23	16.1	10.5	23.1	71	7	9.9	4.1	19.3
Rash	Any	143	12	8.4	4.4	14.2	71	0	0.0	0.0	5.1
	Grade 3	143	0	0.0	0.0	2.5	71	0	0.0	0.0	5.1
	Related	143	4	2.8	0.8	7.0	71	0	0.0	0.0	5.1
Urticaria	Any	143	3	2.1	0.4	6.0	71	1	1.4	0.0	7.6
	Grade 3	143	1	0.7	0.0	3.8	71	0	0.0	0.0	5.1
	Related	143	2	1.4	0.2	5.0	71	1	1.4	0.0	7.6
Dose 3											
Arthralgia	Any	141	14	9.9	5.5	16.1	67	3	4.5	0.9	12.5
	Grade 3	141	0	0.0	0.0	2.6	67	0	0.0	0.0	5.4
	Related	141	6	4.3	1.6	9.0	67	2	3.0	0.4	10.4
Fatigue	Any	141	68	48.2	39.7	56.8	67	15	22.4	13.1	34.2
	Grade 3	141	3	2.1	0.4	6.1	67	0	0.0	0.0	5.4
	Related	141	30	21.3	14.8	29.0	67	7	10.4	4.3	20.3
Fever (Axillary)	≥37.5°C	141	2	1.4	0.2	5.0	67	1	1.5	0.0	8.0
	>39.0°C	141	0	0.0	0.0	2.6	67	0	0.0	0.0	5.4
	Related	141	2	1.4	0.2	5.0	67	0	0.0	0.0	5.4
Gastrointestinal symptoms	Any	141	23	16.3	10.6	23.5	67	2	3.0	0.4	10.4
	Grade 3	141	0	0.0	0.0	2.6	67	0	0.0	0.0	5.4
	Related	141	8	5.7	2.5	10.9	67	1	1.5	0.0	8.0
Headache	Any	141	40	28.4	21.1	36.6	67	8	11.9	5.3	22.2
	Grade 3	141	3	2.1	0.4	6.1	67	0	0.0	0.0	5.4
	Related	141	18	12.8	7.7	19.4	67	1	1.5	0.0	8.0
Myalgia	Any	141	55	39.0	30.9	47.6	67	12	17.9	9.6	29.2
	Grade 3	141	1	0.7	0.0	3.9	67	0	0.0	0.0	5.4
	Related	141	21	14.9	9.5	21.9	67	5	7.5	2.5	16.6
Rash	Any	141	12	8.5	4.5	14.4	67	3	4.5	0.9	12.5
	Grade 3	141	1	0.7	0.0	3.9	67	0	0.0	0.0	5.4
	Related	141	5	3.5	1.2	8.1	67	3	4.5	0.9	12.5
Urticaria	Any	141	4	2.8	0.8	7.1	67	0	0.0	0.0	5.4
	Grade 3	141	0	0.0	0.0	2.6	67	0	0.0	0.0	5.4
	Related	141	2	1.4	0.2	5.0	67	0	0.0	0.0	5.4
Across doses											
Arthralgia	Any	145	35	24.1	17.4	31.9	72	8	11.1	4.9	20.7
	Grade 3	145	2	1.4	0.2	4.9	72	0	0.0	0.0	5.0
	Related	145	13	9.0	4.9	14.8	72	3	4.2	0.9	11.7
Fatigue	Any	145	103	71.0	62.9	78.3	72	39	54.2	42.0	66.0
	Grade 3	145	11	7.6	3.8	13.2	72	0	0.0	0.0	5.0
	Related	145	46	31.7	24.3	40.0	72	19	26.4	16.7	38.1
Fever (Axillary)	≥37.5 °C	145	7	4.8	2.0	9.7	72	2	2.8	0.3	9.7
	>39.0 °C	145	0	0.0	0.0	2.5	72	0	0.0	0.0	5.0
	Related	145	3	2.1	0.4	5.9	72	0	0.0	0.0	5.0
Gastrointestinal symptoms	Any	145	52	35.9	28.1	44.2	72	16	22.2	13.3	33.6
	Grade 3	145	1	0.7	0.0	3.8	72	0	0.0	0.0	5.0
	Related	145	19	13.1	8.1	19.7	72	2	2.8	0.3	9.7
Headache	Any	145	73	50.3	41.9	58.7	72	30	41.7	30.2	53.9
	Grade 3	145	5	3.4	1.1	7.9	72	3	4.2	0.9	11.7
	Related	145	32	22.1	15.6	29.7	72	11	15.3	7.9	25.7

Myalgia	Any	145	97	66.9	58.6	74.5	72	33	45.8	34.0	58.0
	Grade 3	145	3	2.1	0.4	5.9	72	2	2.8	0.3	9.7
	Related	145	49	33.8	26.2	42.1	72	21	29.2	19.0	41.1
Rash	Any	145	29	20.0	13.8	27.4	72	8	11.1	4.9	20.7
	Grade 3	145	1	0.7	0.0	3.8	72	0	0.0	0.0	5.0
	Related	145	13	9.0	4.9	14.8	72	3	4.2	0.9	11.7
Urticaria	Any	145	12	8.3	4.3	14.0	72	2	2.8	0.3	9.7
	Grade 3	145	2	1.4	0.2	4.9	72	0	0.0	0.0	5.0
	Related	145	6	4.1	1.5	8.8	72	1	1.4	0.0	7.5

N = number of subjects with at least one 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) for the Total Vaccinated Cohort

New onset chronic diseases	**HPV Group N = 149**	**ALU Group N = 76**
Subjects with any NOCD, n (%)	5 (3.4)	6 (7.9)
Rhinitis allergic	1 (0.7)	3 (3.9)
Dermatitis atopic	2 (1.3)	1 (1.3)
Urticaria	1 (0.7)	1 (1.3)
Dermatitis contact	1 (0.7)	-
Hyperthyroidism	-	1 (1.3)

- : Adverse event absent

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

Medically significant AEs	**HPV Group N = 149**	**ALU Group N = 76**
Subjects with any medically significant AE(s), n (%)	34 (22.8)	10 (13.2)
Acne	4 (2.7)	-
Dental caries	1 (0.7)	1 (1.3)
Dermatitis atopic	2 (1.3)	-
Diarrhoea	2 (1.3)	-
Folliculitis	1 (0.7)	1 (1.3)
Gastritis	2 (1.3)	-
Gastrooesophageal reflux disease	2 (1.3)	-
Rhinitis allergic	1 (0.7)	1 (1.3)
Abdominal pain	-	1 (1.3)
Acarodermatitis	1 (0.7)	-
Alopecia areata	-	1 (1.3)
Dermatitis	1 (0.7)	-
Dermatitis contact	1 (0.7)	-
Dyspepsia	1 (0.7)	-
Eczema	1 (0.7)	-
Enteritis	-	1 (1.3)
Gastrointestinal disorder	1 (0.7)	-
Herpes virus infection	1 (0.7)	-
Hordeolum	-	1 (1.3)
Human bite	1 (0.7)	-
Hyperthyroidism	-	1 (1.3)
Insomnia	-	1 (1.3)
Joint sprain	1 (0.7)	-

Keratitis	-	1 (1.3)
Lacrimal disorder	1 (0.7)	-
Limb injury	1 (0.7)	-
Musculoskeletal pain	1 (0.7)	-
Nausea	1 (0.7)	-
Neck mass	1 (0.7)	-
Ovarian cyst ruptured	1 (0.7)	-
Pain in extremity	1 (0.7)	-
Pelvic inflammatory disease	1 (0.7)	-
Polycystic ovaries	1 (0.7)	-
Skin laceration	1 (0.7)	-
Skin papilloma	1 (0.7)	-
Subcutaneous nodule	-	1 (1.3)
Thermal burn	1 (0.7)	-
Tinnitus	-	1 (1.3)
Urticaria	1 (0.7)	-
- : Adverse event absent		

Secondary Outcome Variable(s): Number of subjects with pregnancies and their outcomes up to Month 7 (Total Vaccinated Cohort)

Categories	**HPV Group N = 0**		**Alu Group N = 1**	
	n	%	n	%
Elective abortion	0	0.0	1	100

N=number of pregnancy
n(%)= number (percentage) of pregnancy outcomes in a given category.

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 = 149**	**ALU Group N = 76**
Subjects with any AE(s), n (%)	66 (44.3)	19 (25.0)
Subjects with any Grade 3 AE(s), n (%)	3 (2.0)	1 (1.3)
Subjects with any AE(s) that were causally related, n (%)	13 (8.7)	3 (3.9)
Upper respiratory tract infection	20 (13.4)	3 (3.9)
Dysmenorrhea	13 (8.7)	3 (3.9)
Headache	9 (6.0)	4 (5.3)
Injection site pruritus	9 (6.0)	-
Pruritus	3 (2.0)	2 (2.6)
Rhinitis	5 (3.4)	-
Dyspepsia	3 (2.0)	-
Feeling hot	2 (1.3)	1 (1.3)
Injection site warmth	2 (1.3)	1 (1.3)
Rhinitis allergic	-	3 (3.9)
Abdominal pain	2 (1.3)	-
Dermatitis atopic	2 (1.3)	-
Eczema	2 (1.3)	-
Gastrooesophageal reflux disease	2 (1.3)	-
Pharyngitis	-	2 (2.6)
Dental caries	-	1 (1.3)
Dizziness	-	1 (1.3)
Folliculitis	-	1 (1.3)
Hordeolum	-	1 (1.3)
Hyperthyroidism	-	1 (1.3)
Hypoaesthesia	-	1 (1.3)
Malaise	-	1 (1.3)
Metrorrhagia	-	1 (1.3)
Subcutaneous nodule	-	1 (1.3)

Tinnitus	-	1 (1.3)
Urticaria	-	1 (1.3)
- : Adverse event absent or not meeting the selected rule(s) Detail of counting rule: ≤ 3 groups and > 30 patients per group, display 10 most frequent primary preferred terms in each group		
Safety Results: Number (%) of subjects with SAEs reported during the entire study period (Day 0 up to Month 7) for the Total Vaccinated Cohort		
All SAEs	**HPV Group N = 149**	**ALU Group N = 76**
Subjects with any SAE(s), n (%) [n related]	2 (1.3) [0]	1 (1.3) [0]
Gastroenteritis viral	0 (0.0) [0]	1 (1.3) [0]
Ovarian cyst ruptured	1 (0.7) [0]	0 (0.0) [0]
Pelvic inflammatory disease	1 (0.7) [0]	0 (0.0) [0]
Fatal SAEs	**HPV Group N = 149**	**ALU Group N = 76**
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. During the 30-day follow-up period after vaccination, at least one unsolicited AE was reported by 66 (44.3%) subjects in the HPV Group and by 19 (25%) subjects in the ALU Group. During the entire study period, 5 (3.4%) subjects from HPV Group and 6 (7.9%) subjects from ALU Group reported NOCD; 34 (22.8%) subjects from HPV Group and 10 (13.2%) subjects from ALU Group reported a medically significant AE; 3 SAEs were reported by 3 subjects (2 subjects in the HPV Group and 1 subject in the ALU Group). None of the SAEs were considered by the investigator to have a causal relationship to vaccination. There were no fatal events reported throughout the study period.

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.
Kim CS et al. (2011) Human Papillomavirus 16/18 AS04-adjuvanted cervical cancer vaccine: Immunogenicity and Safety in 15–25 year old healthy Korean women. J Gynecol Oncol. 22(2):67-75.

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