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Study No.: 113528 (Flu D-Pan-H1N1-010)
Title: Safety and immunogenicity study of GSK Biologicals' pandemic influenza candidate vaccine (GSK2340272A) in children aged 3 to 17 years. GSK2340272A (Flu Pan): GlaxoSmithKline (GSK) Biologicals' Pandemic influenza vaccine comprising A/California/7/2009 (H1N1)v-like strain.
Rationale: The purpose of the study was to assess the safety and immunogenicity of a prime-boost schedule of Flu Pan vaccine in children aged between 3 to 17 years. This summary presents results on preliminary data up to Day 42 and will be updated when additional data become available. As results are based on preliminary data, the numbers may change when the final data become available.
Phase: III
Study Period: 10 September 2009 to 13 November 2009 (Data lock point at Day 42)
Study Design: Non-randomized, multicenter, open label study with one group stratified by age.
Centers: 5 centers in Spain.
Indication: Immunization of healthy children aged 3 to 17 years against A/California/7/2009 (H1N1)v-like influenza.
Treatment: There was 1 treatment group in this study. Flu Pan Group: Subjects received 2 primary doses of Flu Pan vaccine according to a 0, 21-day schedule and are scheduled to receive 1 booster dose at Month 6. Subjects were allocated to that vaccine regimen according to 3 age strata, with the ratio 1:1:2. <ul style="list-style-type: none"> - 3 to 5 years, - 6 to 9 years, - 10 to 17 years. The vaccine was administered intramuscularly in the deltoid region of the arm.
Objectives: <ul style="list-style-type: none"> • To evaluate the humoral immune response after 2 primary administrations of the Flu Pan vaccine that meets or exceeds the European Medicines Agency (EMA) [Committee for Medicinal Products for Human Use (CHMP)] guidance targets for pandemic vaccine seroconversion rate (SCR), seroprotection rate (SPR) and geometric mean fold rise (GMFR) at 21 days after the second dose of Flu Pan vaccine in children aged 3 to 17 years. Criterion for success: The CHMP criteria are fulfilled if the point estimate for SCR is > 40%, the point estimate for SPR is > 70%, and the point estimate for GMFR is > 2.5 in children aged 3 to 17 years. <ul style="list-style-type: none"> • To evaluate the superiority in terms of vaccine virus homologous haemagglutination inhibition (HI) antibody response of a single dose of the Flu Pan vaccine administered as a 6-month booster after 2-dose primary vaccination compared to the response after the first dose of primary vaccination. Criterion for success: If the lower limit of the two-sided 95% confidence interval (CI) for the geometric mean titer (GMT) ratio (at 7 days after a 6-month booster after 2-dose primary vaccination/21 days after the first dose) is > 2.0.
Primary Outcome/Efficacy Variable: <i>Immunogenicity</i> For the humoral immune response in terms of vaccine H1N1 HI antibodies against A/California/7/2009 (H1N1)v-like virus, the following parameters were calculated with 95% CIs: <i>Observed variable:</i> <ul style="list-style-type: none"> • H1N1 HI antibodies on Day 0, Day 21, Day 42, and at Month 6+7 Days#. <i>Derived variable:</i> <ul style="list-style-type: none"> • GMTs of H1N1 HI antibodies; • SCR* on Day 42; • SPR** on Day 42; • GMFR*** on Day 42. <p>*SCR is defined as the percentage of vaccinees that have either a pre-vaccination titer < 1:10 and a post-vaccination titer ≥ 1:40 or a pre-vaccination titer ≥ 1:10 and at least a four-fold increase in post-vaccination titer. The CHMP criterion is fulfilled</p>

if the point estimate for SCR is > 40% in subjects 18 to 60 years of age. The same criterion was used for this pediatric study.

**SPR is defined as the percentage of vaccinees with a serum HI titer $\geq 1:40$ that usually is accepted as indicating protection. The CHMP criterion is fulfilled if the post-vaccination time point estimate for SPR is > 70% in subjects 18 to 60 years of age. The same criterion was used for this pediatric study.

***GMFR also called seroconversion factor (SCF) is defined as the fold increase in serum HI GMTs post-vaccination compared to pre-vaccination. The criterion is fulfilled if the point estimate for GMFR/SCF is > 2.5 in subjects 18 to 60 years of age. The same criterion was used for this pediatric study.

Data not available at the time of writing the summary. The CTRS will be updated when additional results become available.

Secondary Outcome/Efficacy Variable(s):

Immunogenicity

For the humoral immune response in terms of H1N1 HI antibodies against A/California/7/2009 (H1N1)v-like virus, the following parameters were calculated with 95% CIs:

Observed variable:

- H1N1 HI antibodies on Day 0, Day 21, Day 42, at Month 6[#], Month 6+7 Days[#], Month 12[#], and Month 18[#].

Derived variable:

- GMTs and seropositivity rates;
- SCRs;
- SPRs;
- SCFs;
- Booster SCR*[#];
- Booster SCF**[#].

* Booster SCR: For seronegative subjects at pre-booster (Month 6), antibody titer $\geq 1:40$ at post-booster time points. For seropositive subjects at pre-booster (Month 6), antibody titer at post-booster time points ≥ 4 -fold the pre-booster antibody titer.

** Booster SCF is defined as the fold increase in serum H1N1 HI antibody GMTs post-booster compared to pre-booster (Month 6).

The same analyses as above were performed in each age stratum.

For the humoral immune response in terms of neutralizing antibodies against A/California/7/2009 (H1N1)v-like virus (in a subset of subjects randomly selected), the following parameters were calculated with 95% CIs:

Observed variable:

- Serum neutralizing antibody titers on Day 0, Day 21, Day 42, Month 6[#], Month 6+7 Days[#], Month 12[#], and Month 18[#].

Derived variable:

- GMTs of serum neutralizing antibody titers[#];
- SCRs[#];
- Booster SCR[#].

Safety:

- Percentage, intensity and relationship to vaccination of solicited local and general signs and symptoms during a 7-day follow-up period, i.e., day of vaccination and 6 subsequent days after each vaccination on Day 0, Day 21, and at Month 6[#].
- Percentage, intensity and relationship to vaccination of unsolicited adverse events (AEs) during a 21-day follow-up period after the first vaccination, during a 62-day follow-up period after the second vaccination[#], and during a 30-day follow-up period after the booster vaccination[#].
- Occurrence of medically-attended events (MAEs), adverse event of specific interest (AESIs)/potential immune-mediated disease (pIMDs), serious adverse events (SAEs) and relationship to vaccination as assessed by the investigators during the entire study period.
- The number and percentage of subjects with normal or abnormal values of biochemical parameters on Day 0, Day 21, Day 42, at Month 6[#], and Month 6+7 Days[#].

Data not available at the time of writing the summary. The CTRS will be updated when additional results become available.

Statistical Methods:

The analyses were performed on the Total Vaccinated Cohort and the According-To-Protocol (ATP) cohort for immunogenicity at Day 42.

- The Total Vaccinated Cohort included all vaccinated subjects.
- The ATP cohort for immunogenicity at Day 42 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 2 doses were taken and assay results were available for antibodies against H1N1 antigen for the blood sample taken twenty one days after the second vaccine dose given at Day 21.

The analyses were performed on preliminary data.

Analysis of immunogenicity:

The analysis was performed on the ATP cohort for immunogenicity at Day 42

The HI immune response to Flu Pan vaccine was described by estimating the following parameters (with 95% CI) for each age stratum: GMTs, SPR, SCR and SCF on Day 0, 21 and 42. Antibody titers below the cut-off of the assay were given an arbitrary value of half the cut-off.

Analysis of safety:

The analysis was performed on the Total Vaccinated Cohort.

The incidence of solicited local and general symptoms occurring during a 7-day follow-up period after each vaccination was tabulated with exact 95% CI for each age stratum. The same tabulation was performed for symptoms of any intensity, those with intensity of grade 3, as well as for solicited general symptoms assessed by the investigator as related to vaccination.

The percentage of subjects with at least one report of an unsolicited AE classified by Medical Dictionary for Regulatory Activities (MedDRA) Preferred Term during a 21-day follow-up period following each dose of vaccine was tabulated.

Adverse events with medically attended visits (MAEs) adverse event of specific interest (AESIs)/potential immune-mediated disease (pIMDs) and SAEs were collected and summarized by MedDRA preferred terms up to Day 42.

Study Population: Healthy male or female children between 3 to 17 years of age at the time of first vaccination were included. If the subject was female and if she was of childbearing potential, she had to practice adequate contraception for 30 days prior to vaccination, was to have a negative pregnancy test and had to continue such precautions for 2 months after completion of the vaccination series. Written informed consent was obtained from the subjects' parent(s) or legally acceptable representative(s) [LAR(s)] of the subject. Assent was obtained from the subject when applicable.

		Flu Pan Group									
Number of subjects		3-5Y	6-9Y	10-17Y							
Planned, N		50	50	100							
Randomized, N (Total Vaccinated Cohort)		53	57	100							
Completed, n (%) (Up to Day 21)		53 (100)	57 (100)	97 (97.0)							
Completed, n (%) (Up to Day 42)		53 (100)	56 (98.2)	93 (93.0)							
Total Number Subjects Withdrawn, n (%)		0 (0.0)	1 (1.8)	7 (7.0)							
Withdrawn due to Adverse Events, n (%)		0 (0.0)	0 (0.0)	0 (0.0)							
Withdrawn due to Lack of Efficacy, n (%)		Not applicable	Not applicable	Not applicable							
Withdrawn for other reasons, n (%)		0 (0.0)	1 (1.8)	7 (7.0)							
Demographics		3-5Y	6-9Y	10-17Y							
N (Total Vaccinated Cohort)		53	57	100							
Females: Males		31:22	25:32	61:39							
Mean Age, years (SD)		3.5 (0.70)	7.5 (1.18)	13.3 (2.23)							
White - Caucasian / European heritage, n (%)		53 (100)	56 (98.2)	99 (99.0)							
3-5Y: subjects aged 3 to 5 years											
6-9Y: subjects aged 6 to 9 years											
10-17Y: subjects aged 10 to 17 years											
Primary Efficacy Results: Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/09 stratified by age-strata 3-5 years, 6-9 years and 10-17 years and overall (ATP Cohort for Immunogenicity at Day 42)											
		≥ 1:10			GMT*						
		95% CI			95% CI						
Antibody	Group	Sub-group	Timing	N	n	%	LL	UL	value	LL	UL
Flu A/CAL/7/09.HA1	Flu Pan	3-5Y	PRE	51	0	0.0	0.0	7.0	5.0	5.0	5.0
			PI(21)	51	51	100	93.0	100	245.4	209.3	287.8
			PII(D42)	51	51	100	93.0	100	1924.3	1681.9	2201.6

Ab	6-9Y	PRE	55	7	12.7	5.3	24.5	6.6	5.3	8.1
		PI(21)	55	55	100	93.5	100	386.5	301.9	494.9
		PII(D42)	55	55	100	93.5	100	1479.6	1296.5	1688.5
	10-17Y	PRE	92	33	35.9	26.1	46.5	9.8	7.6	12.7
		PI(21)	92	92	100	96.1	100	711.1	592.0	854.2
		PII(D42)	88	88	100	95.9	100	1384.9	1210.7	1584.1
	Overall	PRE	198	40	20.2	14.8	26.5	7.4	6.4	8.5
		PI(21)	198	198	100	98.2	100	456.5	400.5	520.3
		PII(D42)	194	194	100	98.1	100	1538.5	1419.0	1668.2

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 at Day 0
PI (D21) = Post-vaccination at Day 21
PII (D42) = Post-vaccination at Day 42
* Primary Results

Primary Efficacy Results: Seroconversion rate (SCR) for HI antibodies against Flu A/CAL/7/09.HA1 Ab stratified by age-strata 3-5 years, 6-9 years and 10-17 years and overall (ATP Cohort for Immunogenicity at Day 42)

					SCR*				
					95% CI				
Strain	Group	Sub-group	Timing	N	n	%	LL	UL	
Flu A/CAL/7/09.HA1 Ab	Flu Pan	3-5Y	PI(21)	51	51	100	93.0	100	
			PII(D42)*	51	51	100	93.0	100	
		6-9Y	PI(21)	55	55	100	93.5	100	
			PII(D42)*	55	55	100	93.5	100	
		10-17Y	PI(21)	92	89	96.7	90.8	99.3	
			PII(D42)*	88	85	96.6	90.4	99.3	
		Overall	PI(21)	198	195	98.5	95.6	99.7	
			PII(D42)*	194	191	98.5	95.5	99.7	

Seroconversion defined as:
For initially seronegative subjects, antibody titer \geq 1:40 after vaccination
For initially seropositive subjects, antibody titer after vaccination \geq 4 fold the pre-vaccination antibody titer
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI(D21) = Post-vaccination at Day 21
PII (D42) = Post-vaccination at Day 42
* Primary Results

Primary Efficacy Results: Seroprotection rates (SPR) for HI antibodies against Flu A/CAL/7/09.HA1 Ab stratified by age-strata 3-5 years, 6-9 years and 10-17 years and overall (ATP Cohort for Immunogenicity at Day 42)

					SPR				
					95% CI				
Strain	Group	Sub-group	Timing	N	n	%	LL	UL	
Flu A/CAL/7/09.HA1 Ab	Flu Pan	3-5Y	PRE	51	0	0.0	0.0	7.0	
			PI(21)	51	51	100	93.0	100	
			PII(D42)*	51	51	100	93.0	100	
		6-9Y	PRE	55	4	7.3	2.0	17.6	
			PI(21)	55	55	100	93.5	100	
			PII(D42)*	55	55	100	93.5	100	
		10-17Y	PRE	92	13	14.1	7.7	23.0	
			PI(21)	92	92	100	96.1	100	
			PII(D42)*	88	88	100	95.9	100	
		Overall	PRE	198	17	8.6	5.1	13.4	
PI(21)	198		198	100	98.2	100			

Grade 3 pain in the 3-5 years group = cried when limb was moved/spontaneously painful

Grade 3 pain in the 6-17 years groups = pain that prevented normal activity

N= number of subjects with at least one administered 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): Incidence of solicited general symptoms reported during the 7-day (Days 0-6) following each dose and overall in the 3-5 year-old sub-group (Total Vaccinated Cohort)

Symptom	Type	Flu Pan Group				
		3-5Y			95 % CI	
		N	n	%	LL	UL
Dose 1						
Diarrhea	Any	53	2	3.8	0.5	13.0
	Grade 3	53	0	0.0	0.0	6.7
	Related	53	1	1.9	0.0	10.1
Drowsiness	Any	53	11	20.8	10.8	34.1
	Grade 3	53	0	0.0	0.0	6.7
	Related	53	8	15.1	6.7	27.6
Irritability	Any	53	14	26.4	15.3	40.3
	Grade 3	53	0	0.0	0.0	6.7
	Related	53	10	18.9	9.4	32.0
Loss of appetite	Any	53	14	26.4	15.3	40.3
	Grade 3	53	0	0.0	0.0	6.7
	Related	53	8	15.1	6.7	27.6
Shivering	Any	53	5	9.4	3.1	20.7
	Grade 3	53	0	0.0	0.0	6.7
	Related	53	2	3.8	0.5	13.0
Sweating	Any	53	4	7.5	2.1	18.2
	Grade 3	53	0	0.0	0.0	6.7
	Related	53	1	1.9	0.0	10.1
Temperature/ (Axillary)	≥ 37.5°C	53	14	26.4	15.3	40.3
	> 39°C	53	1	1.9	0.0	10.1
	Related	53	8	15.1	6.7	27.6
Dose 2						
Diarrhea	Any	52	6	11.5	4.4	23.4
	Grade 3	52	0	0.0	0.0	6.8
	Related	52	3	5.8	1.2	15.9
Drowsiness	Any	52	17	32.7	20.3	47.1
	Grade 3	52	2	3.8	0.5	13.2
	Related	52	15	28.8	17.1	43.1
Irritability	Any	52	15	28.8	17.1	43.1
	Grade 3	52	3	5.8	1.2	15.9
	Related	52	14	26.9	15.6	41.0
Loss of appetite	Any	52	21	40.4	27.0	54.9
	Grade 3	52	3	5.8	1.2	15.9
	Related	52	17	32.7	20.3	47.1
Shivering	Any	52	6	11.5	4.4	23.4
	Grade 3	52	1	1.9	0.0	10.3
	Related	52	5	9.6	3.2	21.0
Sweating	Any	52	6	11.5	4.4	23.4
	Grade 3	52	0	0.0	0.0	6.8
	Related	52	4	7.7	2.1	18.5
Temperature/ (Axillary)	≥ 37.5°C	52	26	50.0	35.8	64.2
	> 39°C	52	2	3.8	0.5	13.2

	Related	52	23	44.2	30.5	58.7
Across doses						
Diarrhea	Any	53	8	15.1	6.7	27.6
	Grade 3	53	0	0.0	0.0	6.7
	Related	53	4	7.5	2.1	18.2
Drowsiness	Any	53	22	41.5	28.1	55.9
	Grade 3	53	2	3.8	0.5	13.0
	Related	53	19	35.8	23.1	50.2
Irritability	Any	53	21	39.6	26.5	54.0
	Grade 3	53	3	5.7	1.2	15.7
	Related	53	19	35.8	23.1	50.2
Loss of appetite	Any	53	28	52.8	38.6	66.7
	Grade 3	53	3	5.7	1.2	15.7
	Related	53	21	39.6	26.5	54.0
Shivering	Any	53	11	20.8	10.8	34.1
	Grade 3	53	1	1.9	0.0	10.1
	Related	53	7	13.2	5.5	25.3
Sweating	Any	53	10	18.9	9.4	32.0
	Grade 3	53	0	0.0	0.0	6.7
	Related	53	5	9.4	3.1	20.7
Temperature/ (Axillary)	≥ 37.5°C	53	33	62.3	47.9	75.2
	> 39°C	53	3	5.7	1.2	15.7
	Related	53	26	49.1	35.1	63.2
<p>Any = occurrence of any general symptom regardless of intensity grade and relationship to vaccination Grade 3 = general symptom that prevented normal activity Grade 3 Loss of appetite = not eating at all Related = general symptom assessed by the investigator as causally related to the study vaccination N= number of subjects with at least one administered dose n/= number/percentage of subjects reporting at least once the symptom 95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit</p>						
Secondary Outcome Variable(s): Incidence of solicited general symptoms reported during the 7-day (Days 0-6) following each dose and overall in the 6-9 and 10-17 year-old sub-groups (Total Vaccinated Cohort)						
Symptom	Type	Flu Pan Group				
		6-9Y				
					95 % CI	
		N	n	%	LL	UL
Dose 1						
Arthralgia	Any	57	9	15.8	7.5	27.9
	Grade 3	57	0	0.0	0.0	6.3
	Related	57	8	14.0	6.3	25.8
Fatigue	Any	57	21	36.8	24.4	50.7
	Grade 3	57	1	1.8	0.0	9.4
	Related	57	20	35.1	22.9	48.9
Gastrointestinal	Any	57	13	22.8	12.7	35.8
	Grade 3	57	2	3.5	0.4	12.1
	Related	57	9	15.8	7.5	27.9
Headache	Any	57	25	43.9	30.7	57.6
	Grade 3	57	2	3.5	0.4	12.1
	Related	57	24	42.1	29.1	55.9
Myalgia	Any	57	15	26.3	15.5	39.7
	Grade 3	57	2	3.5	0.4	12.1
	Related	57	13	22.8	12.7	35.8
Shivering	Any	57	7	12.3	5.1	23.7
	Grade 3	57	0	0.0	0.0	6.3

	Related	57	4	7.0	1.9	17.0
Sweating	Any	57	2	3.5	0.4	12.1
	Grade 3	57	0	0.0	0.0	6.3
	Related	57	1	1.8	0.0	9.4
Temperature/(Axillary)	≥ 37.5° C	57	13	22.8	12.7	35.8
	> 39° C	57	0	0.0	0.0	6.3
	Related	57	10	17.5	8.7	29.9
Dose 2						
Arthralgia	Any	57	13	22.8	12.7	35.8
	Grade 3	57	1	1.8	0.0	9.4
	Related	57	13	22.8	12.7	35.8
Fatigue	Any	57	29	50.9	37.3	64.4
	Grade 3	57	3	5.3	1.1	14.6
	Related	57	28	49.1	35.6	62.7
Gastrointestinal	Any	57	9	15.8	7.5	27.9
	Grade 3	57	0	0.0	0.0	6.3
	Related	57	8	14.0	6.3	25.8
Headache	Any	57	26	45.6	32.4	59.3
	Grade 3	57	4	7.0	1.9	17.0
	Related	57	26	45.6	32.4	59.3
Myalgia	Any	57	16	28.1	17.0	41.5
	Grade 3	57	1	1.8	0.0	9.4
	Related	57	16	28.1	17.0	41.5
Shivering	Any	57	14	24.6	14.1	37.8
	Grade 3	57	0	0.0	0.0	6.3
	Related	57	13	22.8	12.7	35.8
Sweating	Any	57	7	12.3	5.1	23.7
	Grade 3	57	0	0.0	0.0	6.3
	Related	57	4	7.0	1.9	17.0
Temperature/(Axillary)	≥ 37.5° C	57	20	35.1	22.9	48.9
	> 39° C	57	1	1.8	0.0	9.4
	Related	57	19	33.3	21.4	47.1
Across doses						
Arthralgia	Any	57	20	35.1	22.9	48.9
	Grade 3	57	1	1.8	0.0	9.4
	Related	57	19	33.3	21.4	47.1
Fatigue	Any	57	35	61.4	47.6	74.0
	Grade 3	57	4	7.0	1.9	17.0
	Related	57	34	59.6	45.8	72.4
Gastrointestinal	Any	57	17	29.8	18.4	43.4
	Grade 3	57	2	3.5	0.4	12.1
	Related	57	14	24.6	14.1	37.8
Headache	Any	57	34	59.6	45.8	72.4
	Grade 3	57	5	8.8	2.9	19.3
	Related	57	34	59.6	45.8	72.4
Myalgia	Any	57	23	40.4	27.6	54.2
	Grade 3	57	2	3.5	0.4	12.1
	Related	57	21	36.8	24.4	50.7
Shivering	Any	57	19	33.3	21.4	47.1
	Grade 3	57	0	0.0	0.0	6.3
	Related	57	15	26.3	15.5	39.7
Sweating	Any	57	9	15.8	7.5	27.9
	Grade 3	57	0	0.0	0.0	6.3
	Related	57	5	8.8	2.9	19.3

Temperature/(Axillary)	≥ 37.5°C	57	27	47.4	34.0	61.0
	> 39°C	57	1	1.8	0.0	9.4
	Related	57	23	40.4	27.6	54.2
Symptom	Type	Flu Pan Group				
		10-17Y				
					95 % CI	
		N	n	%	LL	UL
Dose 1						
Arthralgia	Any	98	26	26.5	18.1	36.4
	Grade 3	98	1	1.0	0.0	5.6
	Related	98	26	26.5	18.1	36.4
Fatigue	Any	98	44	44.9	34.8	55.3
	Grade 3	98	4	4.1	1.1	10.1
	Related	98	40	40.8	31.0	51.2
Gastrointestinal	Any	98	12	12.2	6.5	20.4
	Grade 3	98	1	1.0	0.0	5.6
	Related	98	6	6.1	2.3	12.9
Headache	Any	98	48	49.0	38.7	59.3
	Grade 3	98	3	3.1	0.6	8.7
	Related	98	41	41.8	31.9	52.2
Myalgia	Any	98	35	35.7	26.3	46.0
	Grade 3	98	2	2.0	0.2	7.2
	Related	98	34	34.7	25.4	45.0
Shivering	Any	98	19	19.4	12.1	28.6
	Grade 3	98	0	0.0	0.0	3.7
	Related	98	14	14.3	8.0	22.8
Sweating	Any	98	8	8.2	3.6	15.5
	Grade 3	98	0	0.0	0.0	3.7
	Related	98	5	5.1	1.7	11.5
Temperature/(Axillary)	≥ 37.5°C	98	17	17.3	10.4	26.3
	> 39°C	98	0	0.0	0.0	3.7
	Related	98	15	15.3	8.8	24.0
Dose 2						
Arthralgia	Any	93	34	36.6	26.8	47.2
	Grade 3	93	1	1.1	0.0	5.8
	Related	93	32	34.4	24.9	45.0
Fatigue	Any	93	50	53.8	43.1	64.2
	Grade 3	93	5	5.4	1.8	12.1
	Related	93	48	51.6	41.0	62.1
Gastrointestinal	Any	93	10	10.8	5.3	18.9
	Grade 3	93	0	0.0	0.0	3.9
	Related	93	6	6.5	2.4	13.5
Headache	Any	93	51	54.8	44.2	65.2
	Grade 3	93	5	5.4	1.8	12.1
	Related	93	50	53.8	43.1	64.2
Myalgia	Any	93	47	50.5	40.0	61.1
	Grade 3	93	2	2.2	0.3	7.6
	Related	93	44	47.3	36.9	57.9
Shivering	Any	93	27	29.0	20.1	39.4
	Grade 3	93	1	1.1	0.0	5.8
	Related	93	25	26.9	18.2	37.1
Sweating	Any	93	8	8.6	3.8	16.2
	Grade 3	93	0	0.0	0.0	3.9
	Related	93	7	7.5	3.1	14.9

Temperature/(Axillary)	≥ 37.5°C	93	23	24.7	16.4	34.8
	> 39°C	93	1	1.1	0.0	5.8
	Related	93	16	17.2	10.2	26.4
Across doses						
Arthralgia	Any	98	44	44.9	34.8	55.3
	Grade 3	98	2	2.0	0.2	7.2
	Related	98	43	43.9	33.9	54.3
Fatigue	Any	98	63	64.3	54.0	73.7
	Grade 3	98	9	9.2	4.3	16.7
	Related	98	59	60.2	49.8	70.0
Gastrointestinal	Any	98	16	16.3	9.6	25.2
	Grade 3	98	1	1.0	0.0	5.6
	Related	98	10	10.2	5.0	18.0
Headache	Any	98	70	71.4	61.4	80.1
	Grade 3	98	6	6.1	2.3	12.9
	Related	98	64	65.3	55.0	74.6
Myalgia	Any	98	56	57.1	46.7	67.1
	Grade 3	98	4	4.1	1.1	10.1
	Related	98	53	54.1	43.7	64.2
Shivering	Any	98	38	38.8	29.1	49.2
	Grade 3	98	1	1.0	0.0	5.6
	Related	98	33	33.7	24.4	43.9
Sweating	Any	98	14	14.3	8.0	22.8
	Grade 3	98	0	0.0	0.0	3.7
	Related	98	11	11.2	5.7	19.2
Temperature/(Axillary) (°C)	≥ 37.5°C	98	33	33.7	24.4	43.9
	> 39°C	98	1	1.0	0.0	5.6
	Related	98	25	25.5	17.2	35.3

Any = occurrence of any general symptom regardless of intensity grade and relationship to vaccination

Grade 3 = general symptom that prevented normal activity

Related = general symptom assessed by the investigator as causally related to the study vaccination

N= number of subjects with at least one administered 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 reporting the occurrence of unsolicited adverse events with medically attended visit (MAEs), up to Day 42 (Total Vaccinated Cohort)

Most frequent MAEs	Flu Pan Group		
	3-5Y N = 53	6-9Y N = 57	10-17Y N = 100
Subjects with any MAE(s), n (%)	20 (37.7)	6 (10.5)	10 (10.0)
Motion sickness	-	-	1 (1.0)
Conjunctivitis	-	1 (1.8)	-
Keratitis	1 (1.9)	-	-
Stomatitis	-	-	1 (1.0)
Bronchitis	1 (1.9)	-	-
Ear infection	2 (3.8)	-	-
Gastroenteritis	2 (3.8)	-	-
Influenza	1 (1.9)	-	-
Laryngitis	5 (9.4)	2 (3.5)	-
Molluscum contagiosum	1 (1.9)	-	-
Nasopharyngitis	-	1 (1.8)	-
Otitis externa	1 (1.9)	-	-
Otitis media	2 (3.8)	-	-
Otitis media acute	1 (1.9)	-	-

ASAT	PRE	59	0	0.0	0	0.0	58	98.3	1	1.7
	PI(21)	97	2	2.1	0	0.0	94	96.9	1	1.0
	PII(D42)	93	0	0.0	0	0.0	91	97.8	2	2.2
Bilirubin	PRE	59	0	0.0	0	0.0	57	96.6	2	3.4
		59	0	0.0	0	0.0	58	98.3	1	1.7
	PI(21)	97	2	2.1	0	0.0	90	92.8	5	5.2
		97	2	2.1	0	0.0	94	96.9	1	1.0
	PII(D42)	93	0	0.0	0	0.0	90	96.8	3	3.2
		93	0	0.0	0	0.0	93	100	0	0.0
Creatinine	PRE	59	0	0.0	1	1.7	54	91.5	4	6.8
	PI(21)	97	2	2.1	1	1.0	90	92.8	4	4.1
	PII(D42)	93	0	0.0	2	2.2	85	91.4	6	6.5
BUN	PRE	59	0	0.0	0	0.0	57	96.6	2	3.4
	PI(21)	97	2	2.1	0	0.0	92	94.8	3	3.1
	PII(D42)	93	0	0.0	0	0.0	89	95.7	4	4.3

N = number of subjects with available results
n/%= number/percentage of subjects in the specified category

BUN = Blood Urea Nitrogen;

ALAT = Alanine Amino Transferase;

ASAT = Aspartate Amino Transferase;

BILI = Bilirubin;

CREA = Creatinine

PRE (D0) = pre-vaccination at Day 0

PI (21) = post-vaccination at Day 21

PII (D42) = post-vaccination at Day 42

Safety Results: Number (%) of subjects with unsolicited adverse events (Total Vaccinated Cohort)

Most frequent adverse events - On-Therapy (occurring within Day 0-20 following vaccination)	Flu Pan Group		
	3-5Y N = 53	6-9Y N = 57	10-17Y N = 100
Subjects with any AE(s), n (%)	29 (54.7)	22 (38.6)	30 (30.0)
Subjects with grade 3 AE(s), n (%)	4 (7.5)	2 (3.5)	1 (1.0)
Subjects with related AE(s), n (%)	2 (3.8)	4 (7.0)	6 (6.0)
Upper respiratory tract infection	10 (18.9)	3 (5.3)	10 (10.0)
Cough	3 (5.7)	3 (5.3)	3 (3.0)
Laryngitis	5 (9.4)	2 (3.5)	-
Dizziness	-	2 (3.5)	2 (2.0)
Headache	2 (3.8)	-	2 (2.0)
Gastroenteritis	2 (3.8)	-	1 (1.0)
Oropharyngeal pain	-	3 (5.3)	-
Pharyngitis	2 (3.8)	-	1 (1.0)
Pyrexia	2 (3.8)	-	1 (1.0)
Vomiting	2 (3.8)	1 (1.8)	-
Acne	-	-	2 (2.0)
Axillary pain	-	1 (1.8)	1 (1.0)
Bronchitis	-	-	2 (2.0)
Ear infection	2 (3.8)	-	-
Face injury	-	2 (3.5)	-
Nasal congestion	-	1 (1.8)	1 (1.0)
Nasopharyngitis	-	2 (3.5)	-
Otitis media	2 (3.8)	-	-
Tonsillitis	-	-	2 (2.0)
Urticaria	-	1 (1.8)	1 (1.0)
Anxiety	-	-	1 (1.0)
Attention deficit/hyperactivity disorder	-	-	1 (1.0)

Bronchospasm	-	-	1 (1.0)
Chills	-	-	1 (1.0)
Conjunctivitis	-	1 (1.8)	-
Decreased appetite	-	1 (1.8)	-
Dyslalia	-	-	1 (1.0)
Dyspnoea	-	-	1 (1.0)
Ear pain	-	1 (1.8)	-
Epistaxis	-	-	1 (1.0)
Fatigue	-	-	1 (1.0)
Gastrointestinal disorder	-	-	1 (1.0)
Gingival erythema	-	1 (1.8)	-
Hordeolum	-	-	1 (1.0)
Inflammation	-	-	1 (1.0)
Injection site nodule	-	1 (1.8)	-
Insomnia	-	-	1 (1.0)
Lymphadenopathy	-	-	1 (1.0)
Malaise	-	-	1 (1.0)
Motion sickness	-	-	1 (1.0)
Odynophagia	-	1 (1.8)	-
Oral herpes	-	1 (1.8)	-
Oral pain	-	1 (1.8)	-
Pyoderma	-	-	1 (1.0)
Radius fracture	-	1 (1.8)	-
Rhinitis	-	1 (1.8)	-
Rhinorrhoea	-	1 (1.8)	-
Stomatitis	-	-	1 (1.0)
Synovitis	-	-	1 (1.0)
Viral infection	-	-	1 (1.0)
- : Adverse event absent or not meeting the selected rule: more than 30 subjects per group and ≤ 3 group: display the 10 most frequent adverse events in each group Grade 3= event that prevented normal activities Related= event assessed by the investigator as causally related to the study vaccination			
Safety Results: Number (%) of subjects with serious adverse events up to Day 42 (Total Vaccinated Cohort)			
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]			
	Flu Pan Group		
All SAEs	3-5Y N = 53	6-9Y N = 57	10-17Y N = 100
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Fatal SAEs	3-5Y	6-9Y	10-17Y
Subjects with fatal SAE (s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]

Conclusion: At Day 21 across age groups, GMT value for HI antibodies against Flu A/CAL/7/09 was 456.5; 21 days after the second dose (Day 42), the GMT value was 1538.5. At the same time point, the SCR was 98.5%, the SPR was 100% and the SCF value was 208.5.
At least one unsolicited adverse event was reported by 29 (54.7%) subjects in the 3-5 years subgroup, 22 (38.6%) subjects in the 6-9 years subgroup and 30 (30.0%) subjects in the 10-17 years subgroup. No SAEs were reported up to Day 42.

Publications: None.

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