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Study No.: 113572 (FLU D-PAN H1N1-020)
Title: Immunogenicity and safety of GSK Biologicals' pandemic influenza candidate vaccine GSK2340272A GSK234072A (H1N1): GlaxoSmithKline (GSK) Biologicals' Pandemic influenza vaccine comprising A/California/7/2009 (H1N1)v-like strain.
Rationale: The aim of the study was to assess the immunogenicity and safety of a two-dose schedule with H1N1 vaccine with or without previous administration of Fluarix™ in subjects aged 61 years and older. Fluarix™ (Flu S): GSK Biologicals' licensed seasonal Trivalent Influenza Vaccine (TIV) This summary presents results up to Day 21 on preliminary data 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: From 08 September 2009 to 26 October 2009 (data lock point Day 21)
Study Design: Randomized (1:1), single-blind with 2 parallel groups.
Centres: 6 centres in Germany.
Indication: Immunization against A/California/7/2009 (H1N1)v-like influenza in male and female subjects aged 61 years or above.
Treatment: Study groups were as follows: <ul style="list-style-type: none"> • Group A: Subjects received 1 placebo dose at Day -21 (Visit 1), 2 doses of H1N1 vaccine, 1 at Day 0 & 1 at Day 21 (Visits 2 and 3) and 1 dose of Flu S vaccine at Day 42 (Visit 4). • Group B: Subjects received 1 dose of Flu S vaccine at Day -21 (Visit 1), 2 doses of H1N1 vaccine 1 at Day 0 & 1 at Day 21 (Visits 2 and 3) and 1 dose of placebo at Day 42, after the second H1N1 vaccine dose (Visit 4). Vaccines were administered intramuscularly in the deltoid region of the dominant (Flu and Placebo) or non-dominant (H1N1) arm.
Objectives: To assess whether vaccination with 2 doses of the H1N1 vaccine results in an HI immune response that meets or exceeds the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) guidance targets for pandemic influenza vaccines (seroconversion rate (SCR), seroprotection rate (SPR), and seroconversion factor (SCF)) at 21 days after the second dose of H1N1 vaccine when Flu has been administered or not at least 21 days before in subjects aged 61 years and older.
Primary Outcome/Efficacy Variable: <i>Humoral immune response in terms of Haemagglutination Inhibition (HI) antibodies</i> <ul style="list-style-type: none"> • HI antibodies against the vaccine-strain at Day 42#. Derived variables [with 95% Confidence Intervals (CI) for each study group]: <ul style="list-style-type: none"> • Geometric mean titres (GMTs) and seropositivity rates of HI antibody titres at Day 42#. • Seroconversion rate (SCR*) at Day 42#. • Seroconversion factor (SCF**) at Day 42#. • Seroprotection rate (SPR***) at Day 42#. *SCR for HI antibody response is defined as the percentage of subjects who have either a prevaccination (Day -21) titre < 1:10 and a post-vaccination titre ≥ 1:40 or a prevaccination titre ≥ 1:10 and at least a 4-fold increase in post-vaccination titre. **SCF is defined as the fold increase in serum HI antibody GMTs post-vaccination compared to prevaccination (Day -21). ***SPR is defined as the percentage of subjects with a serum HI antibody titre ≥ 1:40 that usually is accepted as indicating protection. The CHMP criteria in subjects > 60 years of age are fulfilled if the point estimate for SCR ≥ 30%, the point estimate for SPR is ≥ 60% and the point estimate for SCF is ≥ 2.0. # At the time of writing this summary, data were available up to Day 21 only. This summary will be updated when additional results become available.
Secondary Outcome/Efficacy Variable(s): <i>Humoral immune response in terms of HI antibodies</i> <ul style="list-style-type: none"> • HI antibodies against vaccine strain at Day -21, Day 0, Day 21, Day 42#, Day 63#, Month 6# and Month 12#. Derived variables (with 95% CI for each study group): <ul style="list-style-type: none"> • GMTs and seropositivity rates of HI antibodies at Day -21, Day 0, Day 21, Day 42#, Day 63#, Month 6# and Month 12#. • SCR* at Day 0, Day 21, Day 42#, Day 63#, Month 6# and Month 12#.

- SCF* at Day 0, Day 21, Day 42[#], Day 63[#], Month 6[#] and Month 12[#].
 - SPR* at Day -21, Day 0, Day 21, Day 42[#], Day 63[#], Month 6[#] and Month 12[#].
- *Criteria for evaluation were the same as that for the primary outcome variables.

Safety

- Occurrence of solicited local signs and symptoms, intensity and duration during a 7-Day follow-up period (i.e. Day of vaccination and 6 subsequent days) after each vaccination[#].
- Occurrence of solicited general signs and symptoms, intensity, duration and relationship to vaccination during a 7-Day follow-up period (i.e. Day of vaccination and 6 subsequent days) after each vaccination[#].
- Occurrence of unsolicited adverse events, intensity[§] and relationship to vaccination[§] during the 21 days after each vaccination[#].
- Occurrence of SAEs, relationship to vaccination during the entire study period[#].
- Occurrence of AEs of specific interest (AESIs), during the entire study period[#].

[#] At the time of writing this summary, data were available up to Day 21 only. This summary will be updated when additional results become available.

[§] Not available at the time of writing this summary.

Statistical Methods:

Analyses were performed on the Total vaccinated cohort (TVC).

- The Total vaccinated cohort included all subjects with at least 1 vaccine administration documented.

The analyses were performed on preliminary data.

Analysis of immunogenicity:

The analysis was based on the Total vaccinated cohort. For the analysis of immunogenicity, this included vaccinated subjects for whom data concerning immunogenicity data were available. The analysis of immunogenicity was done as a descriptive analysis of the humoral immune response in adults 61 years or above.

For the humoral immune response in terms of H1N1 HI antibodies (with 95% confidence intervals [CIs]), for each treatment group, the following parameters were calculated:

- GMTs of H1N1 HI antibody titres at Day -21, Day 0 and Day 21.
- SCR at Day 0 and Day 21.
- SCF at Day 0 and Day 21.
- SPR at Day -21, Day 0 and Day 21.

Analysis of safety:

The analysis was based on the Total vaccinated cohort.

The incidence of solicited local and general symptoms occurring during the 7 days after the first vaccination was tabulated with exact 95% CI for each treatment group. The same calculations were 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. All solicited local AEs were assessed as causally related to the vaccination. Duration of local and general symptoms was also calculated.

The percentages of subjects with at least one report of an unsolicited AE classified by Medical Dictionary for Regulatory Activities (MedDRA) preferred term up to 21 days after the first vaccination were tabulated with exact 95% CI for each treatment group.

SAEs and AESIs were collected and summarized by MedDRA preferred terms.

Study Population: Male or female adults aged 61 years and above at the time of first vaccination with satisfactory baseline medical assessment by history and physical examination. A written informed consent was obtained from the subjects prior to study entry.

Number of Subjects:	Group A	Group B
Planned, N	72	72
Randomised, N (Total Vaccinated Cohort)	72	73
Completed, n (%) (Day 21)	72 (100)	72 (98.6)
Total Number Subjects Withdrawn, n (%)	0 (0.0)	0 (0.0)
Withdrawn due to Adverse Events n (%)	0 (0.0)	0 (0.0)
Withdrawn due to Lack of Efficacy n (%)	Not applicable	Not applicable
Withdrawn for other reasons n (%)	0 (0.0)	0 (0.0)
Demographics	Group A	Group B
N (Total Vaccinated Cohort)	72	73
Females: Males	39:33	34:39
Mean Age, years (SD)	69.1 (5.16)	69.7 (5.59)

White-Caucasian/European heritage, n (%)				71 (98.6)				73 (100)			
Primary Efficacy Results: Not yet available											
Secondary Outcome Variable(s): Geometric mean titres (GMTs) and seropositivity rates for HI antibodies against Flu A/CAL/7/09.HA1 antibody strain (H1N1) at each time point (Total vaccinated cohort)											
				≥ 1:10				GMT			
Antibody	Group	Timing	N	n	%	LL	UL	value	LL	UL	
Flu A/CAL/7/09.HA1	Group A	PI(D -21)	72	25	34.7	23.9	46.9	8.5	6.9	10.6	
		PI(D0)	72	29	40.3	28.9	52.5	8.9	7.2	11.1	
		PII(D21)	72	72	100	95.0	100	148.1	113.6	193.1	
	Group B	PI(D -21)	73	24	32.9	22.3	44.9	7.8	6.5	9.3	
		PI(D0)	72	54	75.0	63.4	84.5	14.3	11.6	17.7	
		PII(D21)	72	72	100	95.0	100	112.5	84.3	150.3	
GMT = geometric mean antibody titre calculated on all subjects N = number of subjects with pre-vaccination results available n/% = number/percentage of subjects with titre above the specified cut-off 95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit PI (D -21) = Vaccination with Placebo or Flu S at Day -21 PI (D0) = Pre-vaccination at Day 0 PII (D21) = Post-vaccination at Day 21											
Secondary Outcome Variable(s): Geometric mean titres (GMTs) and seropositivity rates for HI antibodies against Flu A/Bri/59/07.HA1 antibody strain (Flu S) at each time point (Total vaccinated cohort)											
				≥ 1:10				GMT			
Antibody	Group	Timing	N	n	%	LL	UL	value	LL	UL	
Flu A/Bri/59/07.HA1	Group A	PI(D -21)	72	60	83.3	72.7	91.1	20.5	16.6	25.2	
		PI(D0)	72	61	84.7	74.3	92.1	20.3	16.5	24.9	
	Group B	PI(D -21)	73	58	79.5	68.4	88.0	17.0	13.8	21.0	
		PI(D0)	72	72	100	95.0	100	55.4	43.7	70.3	
GMT = geometric mean antibody titre calculated on all subjects N = number of subjects with pre-vaccination results available n/% = number/percentage of subjects with titre above the specified cut-off 95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit PI (D -21) = Vaccination with Placebo or Flu S at Day -21 PI (D0) = Pre-vaccination at Day 0											
Secondary Outcome Variable(s): Geometric mean titres (GMTs) and seropositivity rates for HI antibodies against Flu B/Bri/08.HA antibody strain (Flu S) at each time point (Total vaccinated cohort)											
				≥ 1:10				GMT			
Antibody	Group	Timing	N	n	%	LL	UL	value	LL	UL	
FluB/Bri/08.HA	Group A	PI(D -21)	72	72	100	95.0	100	121.1	100.3	146.0	
		PI(D0)	72	72	100	95.0	100	117.0	97.8	140.0	
	Group B	PI(D -21)	73	73	100	95.1	100	134.9	107.6	169.1	
		PI(D0)	72	72	100	95.0	100	348.9	286.8	424.5	
GMT = geometric mean antibody titre calculated on all subjects N = number of subjects with pre-vaccination results available n/% = number/percentage of subjects with titre above the specified cut-off 95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit PI (D -21) = Vaccination with Placebo or Flu S at Day -21 PI (D0) = Pre-vaccination at Day 0											
Secondary Outcome Variable(s): Geometric mean titres (GMTs) and seropositivity rates for HI antibodies against Flu A/Uru/07.HA3 antibody strain (Flu S) at each time point (Total vaccinated cohort)											
				≥ 1:10				GMT			
Antibody	Group	Timing	N	n	%	LL	UL	value	LL	UL	
Flu A/Uru/07.HA3	Group A	PI(D -21)	72	59	81.9	71.1	90.0	28.4	21.2	38.0	
		PI(D0)	72	59	81.9	71.1	90.0	27.7	20.8	36.9	
	Group B	PI(D -21)	73	57	78.1	66.9	86.9	23.5	17.1	32.2	
		PI(D0)	72	71	98.6	92.5	100	103.2	78.5	135.5	

<p>GMT = geometric mean antibody titre calculated on all subjects N = number of subjects with pre-vaccination results available n/% = number/percentage of subjects with titre above the specified cut-off 95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit PI (D -21) = Vaccination with Placebo or Flu S at Day -21 PI (D0) = Pre-vaccination at Day 0</p>							
Secondary Outcome Variable(s): Seroconversion rates (SCR) for HI antibodies against Flu A/CAL/7/09.HA1 antibody strain (H1N1) at each time point (Total vaccinated cohort)							
				SCR			
						95% CI	
Strain	Group	Timing	N	n	%	LL	UL
Flu A/CAL/7/09.HA1	Group A	PII(D21)	72	64	88.9	79.3	95.1
	Group B	PII(D21)	72	47	65.3	53.1	76.1
<p>Seroconversion defined as: For initially seronegative subjects, antibody titre \geq 1:40 at 21 days post dose 2 For initially seropositive subjects, antibody titre after vaccination \geq 4 fold the pre-vaccination antibody titre 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 PII (D21) = Post-vaccination at Day 21</p>							
Secondary Outcome Variable(s): Seroconversion rates (SCR) for HI antibodies against Flu A/Bri/59/07.HA1 antibody strain (Flu S) at each time point (Total vaccinated cohort)							
				SCR			
						95% CI	
Strain	Group	Timing	N	n	%	LL	UL
Flu A/Bri/59/07.HA1	Group A	PI (D0)	72	0	0.0	0.0	5.0
	Group B	PI (D0)	72	23	31.9	21.4	44.0
<p>Seroconversion defined as: For initially seronegative subjects, antibody titre \geq 1:40 after vaccination For initially seropositive subjects, antibody titre after vaccination \geq 4 fold the pre-vaccination antibody titre 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 (D0) = Pre-vaccination at Day 0</p>							
Secondary Outcome Variable(s): Seroconversion rates (SCR) for HI antibodies against Flu A/Uru/07.HA3 antibody strain of Flu S at each time point (Total vaccinated cohort)							
				SCR			
						95% CI	
Strain	Group	Timing	N	n	%	LL	UL
Flu A/Uru/07.HA3	Group A	PI(D0)	72	0	0.0	0.0	5.0
	Group B	PI(D0)	72	36	50.0	38.0	62.0
<p>Seroconversion defined as: For initially seronegative subjects, antibody titre \geq 1:40 after vaccination For initially seropositive subjects, antibody titre after vaccination \geq 4 fold the pre-vaccination antibody titre 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 (D0) = Pre-vaccination at Day 0</p>							
Secondary Outcome Variable(s): Seroconversion rates (SCR) for HI antibodies against FluB/Bri/08.HA antibody strain of Flu S at each time point (Total vaccinated cohort)							
				SCR			
						95% CI	
Strain	Group	Timing	N	n	%	LL	UL
Flu B/Bri/08.HA	Group A	PI(D0)	72	1	1.4	0.0	7.5
	Group B	PI(D0)	72	19	26.4	16.7	38.1
Seroconversion defined as:							

<p>For initially seronegative subjects, antibody titre $\geq 1:40$ after vaccination For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre 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 (D0) = Pre-vaccination at Day 0</p>						
<p>Secondary Outcome Variable(s): Geometric mean fold rise (GMFR) for HI antibodies against Flu A/CAL/7/09.HA1 antibody strain (H1N1) at Day 21 (Total vaccinated cohort)</p>						
				GMFR		
					95% CI	
Strain	Group	Timing	N	Value	LL	UL
Flu A/CAL/7/09.HA1(1/DIL)	Group A	PI(D21)	72	16.6	12.9	21.3
	Group B	PI(D21)	72	7.9	5.8	10.6
<p>N = Number of subjects with pre- and post-vaccination results available GMFR = Seroconversion Factor or geometric mean ratio (mean[log10(POST/PRE)]) 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PI (D21) = Post-vaccination at Day 21</p>						
<p>Secondary Outcome Variable(s): Geometric mean fold rise (GMFR) for HI antibodies against Flu A/Bri/59/07.HA1 antibody strain of Flu S at each time point (Total vaccinated cohort)</p>						
				GMFR		
					95% CI	
Strain	Group	Timing	N	Value	LL	UL
Flu A/Bri/59/07.HA1(1/DIL)	Group A	PI(D0)	72	1.0	0.9	1.0
	Group B	PI(D0)	72	3.3	2.5	4.4
<p>N = Number of subjects with pre- and post-vaccination results available GMFR = Seroconversion Factor or geometric mean ratio (mean[log10(POST/PRE)]) 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PI (D0) = Pre-vaccination at Day 0</p>						
<p>Secondary Outcome Variable(s): Geometric mean fold rise (GMFR) for HI antibodies against Flu A/Uru/07.HA3 antibody strain of Flu S at each time point (Total vaccinated cohort)</p>						
				GMFR		
					95% CI	
Strain	Group	Timing	N	Value	LL	UL
Flu A/Uru/07.HA3 (1/DIL)	Group A	PI(D0)	72	1.0	0.9	1.0
	Group B	PI(D0)	72	4.4	3.3	5.9
<p>N = Number of subjects with pre- and post-vaccination results available GMFR = Seroconversion Factor or geometric mean ratio (mean[log10(POST/PRE)]) 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PI (D0) = Pre-vaccination at Day 0</p>						
<p>Secondary Outcome Variable(s): Geometric mean fold rise (GMFR) for HI antibodies against FluB/Bri/08.HA antibody strain of Flu S at each time point (Total vaccinated cohort)</p>						
				GMFR		
					95% CI	
Strain	Group	Timing	N	Value	LL	UL
Flu B/Bri/08.HA1(1/DIL)	Group A	PI(D0)	72	1.0	0.9	1.0
	Group B	PI(D0)	72	2.6	2.1	3.2
<p>N = Number of subjects with pre- and post-vaccination results available GMFR = Seroconversion Factor or geometric mean ratio (mean[log10(POST/PRE)]) 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PI (D0) = Pre-vaccination at Day 0</p>						
<p>Secondary Outcome Variable(s): Seroprotection rates (SPR) for HI antibodies against Flu A/CAL/7/09.HA1 antibody strain (H1N1) at Day 21 (Total vaccinated cohort)</p>						
				SPR		
					95% CI	
Strain	Group	Timing	N	n	%	UL
Flu A/CAL/7/09.HA1	Group A	PI(D -21)	72	9	12.5	22.4

		PI(D0)	72	9	12.5	5.9	22.4
		PII(D21)	72	67	93.1	84.5	97.7
	Group B	PI(D -21)	72	5	6.9	2.3	15.5
		PI(D0)	72	13	18.1	10.0	28.9
		PII(D21)	72	62	86.1	75.9	93.1

N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titre \geq 1:40)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI (D -21) = Vaccination with Placebo or Flu S at Day -21
PI (D0) = Pre-vaccination at Day 0
PII (D21) = Post-vaccination at Day 21

Secondary Outcome Variable(s): Seroprotection rates (SPR) for HI antibodies against Flu A/Bri/59/07.HA1 antibody strain of Flu S at each time point (Total vaccinated cohort)

Strain	Group	Timing	N	n	%	SPR	
						LL	UL
Flu A/Bri/59/07.HA1	Group A	PI(D -21)	72	26	36.1	25.1	48.3
		PI(D0)	72	25	34.7	23.9	46.9
	Group B	PI(D -21)	73	18	24.7	15.3	36.1
		PI(D0)	72	45	62.5	50.3	73.6

N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titre \geq 1:40)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI (D -21) = Vaccination with Placebo or Flu S at Day -21
PI (D0) = Pre-vaccination at Day 0

Secondary Outcome Variable(s): Seroprotection rates (SPR) for HI antibodies against Flu A/Uru/07.HA3 antibody strain of Flu S at each time point (Total vaccinated cohort)

Strain	Group	Timing	N	n	%	SPR	
						LL	UL
Flu A/Uru/07.HA3	Group A	PI(D -21)	72	36	50.0	38.0	62.0
		PI(D0)	72	35	48.6	36.7	60.7
	Group B	PI(D -21)	73	25	34.2	23.5	46.3
		PI(D0)	72	62	86.1	75.9	93.1

N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titre \geq 1:40)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI (D -21) = Vaccination with Placebo or Flu S at Day -21
PI (D0) = Pre-vaccination at Day 0

Secondary Outcome Variable(s): Seroprotection rates (SPR) for HI antibodies against FluB/Bri/08.HA antibody strain of Flu S at each time point (Total vaccinated cohort)

Strain	Group	Timing	N	n	%	SPR	
						LL	UL
Flu B/Bri/08.HA	Group A	PI(D -21)	72	69	95.8	88.3	99.1
		PI(D0)	72	69	95.8	88.3	99.1
	Group B	PI(D -21)	73	69	94.5	86.6	98.5
		PI(D0)	72	72	100	95.0	100

N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titre \geq 1:40)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI (D -21) = Vaccination with Placebo or Flu S at Day -21
PI (D0) = Pre-vaccination at Day 0

Secondary Outcome Variable(s): Incidence of solicited local symptoms reported during the 7-day (Day -21 to Day -15) post-vaccination with Placebo or Flu S (Total Vaccinated Cohort)

		Group A	Group B
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Symptom	Type	N	n	%	95% CI		N	n	%	95% CI																																																																																						
					LL	UL				LL	UL																																																																																					
Pain	All	72	5	6.9	2.3	15.5	72	12	16.7	8.9	27.3																																																																																					
	Grade 3	72	0	0.0	0.0	5.0	72	0	0.0	0.0	5.0																																																																																					
Redness (mm)	All	72	2	2.8	0.3	9.7	72	1	1.4	0.0	7.5																																																																																					
	> 100	72	0	0.0	0.0	5.0	72	1	1.4	0.0	7.5																																																																																					
Swelling (mm)	All	72	0	0.0	0.0	5.0	72	1	1.4	0.0	7.5																																																																																					
	> 100	72	0	0.0	0.0	5.0	72	0	0.0	0.0	5.0																																																																																					
Any= occurrence of any local symptom regardless of intensity grade Grade 3 pain: pain that prevented normal activity N= number of subjects with the documented dose n/= number/percentage of subjects reporting at least once the symptom when the intensity is maximum 95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit																																																																																																
Secondary Outcome Variable(s): Incidence of solicited local symptoms reported during the 7-day (Days 0 – 6) post-vaccination period following first dose of H1N1 candidate vaccine (Total Vaccinated Cohort)																																																																																																
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Symptom	Type	Group A					Group B				
		N	n	%	95 % CI		N	n	%	95 % CI	
					LL	UL				LL	UL
Fatigue	Any	72	9	12.5	5.9	22.4	72	7	9.7	4.0	19.0
	Grade 3	72	1	1.4	0.0	7.5	72	0	0.0	0.0	5.0
	Related	72	6	8.3	3.1	17.3	72	6	8.3	3.1	17.3
Headache	Any	72	5	6.9	2.3	15.5	72	10	13.9	6.9	24.1
	Grade 3	72	0	0.0	0.0	5.0	72	0	0.0	0.0	5.0
	Related	72	3	4.2	0.9	11.7	72	8	11.1	4.9	20.7
Joint pain at other location	Any	72	7	9.7	4.0	19.0	72	2	2.8	0.3	9.7
	Grade 3	72	1	1.4	0.0	7.5	72	1	1.4	0.0	7.5
	Related	72	4	5.6	1.5	13.6	72	2	2.8	0.3	9.7
Muscle aches	Any	72	4	5.6	1.5	13.6	72	6	8.3	3.1	17.3
	Grade 3	72	0	0.0	0.0	5.0	72	1	1.4	0.0	7.5
	Related	72	3	4.2	0.9	11.7	72	5	6.9	2.3	15.5
Shivering	Any	72	2	2.8	0.3	9.7	72	4	5.6	1.5	13.6
	Grade 3	72	0	0.0	0.0	5.0	72	1	1.4	0.0	7.5
	Related	72	2	2.8	0.3	9.7	72	3	4.2	0.9	11.7
Sweating	Any	72	5	6.9	2.3	15.5	72	6	8.3	3.1	17.3
	Grade 3	72	0	0.0	0.0	5.0	72	2	2.8	0.3	9.7
	Related	72	3	4.2	0.9	11.7	72	4	5.6	1.5	13.6
Temperature/(Axillary) (°C)	≥ 38°C	72	0	0.0	0.0	5.0	72	1	1.4	0.0	7.5
	≥ 39°C	72	0	0.0	0.0	5.0	72	1	1.4	0.0	7.5
	Related	72	0	0.0	0.0	5.0	72	1	1.4	0.0	7.5

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

Grade 3 = event that prevented normal activities

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

N= number of subjects with the 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): Incidence of solicited general symptoms reported during the 7-day (Days 0 – 6) post-vaccination period following first dose of H1N1 candidate vaccine (Total Vaccinated Cohort)

Symptom	Type	Group A					Group B				
		N	n	%	95 % CI		N	n	%	95 % CI	
					LL	UL				LL	UL
Fatigue	Any	71	13	18.3	10.1	29.3	71	10	14.1	7.0	24.4
	Grade 3	71	2	2.8	0.3	9.8	71	0	0.0	0.0	5.1
	Related	71	12	16.9	9.0	27.7	71	8	11.3	5.0	21.0
Headache	Any	71	14	19.7	11.2	30.9	71	9	12.7	6.0	22.7
	Grade 3	71	2	2.8	0.3	9.8	71	0	0.0	0.0	5.1
	Related	71	14	19.7	11.2	30.9	71	8	11.3	5.0	21.0
Joint pain at other location	Any	71	11	15.5	8.0	26.0	71	4	5.6	1.6	13.8
	Grade 3	71	2	2.8	0.3	9.8	71	0	0.0	0.0	5.1
	Related	71	8	11.3	5.0	21.0	71	4	5.6	1.6	13.8
Muscle aches	Any	71	15	21.1	12.3	32.4	71	15	21.1	12.3	32.4
	Grade 3	71	2	2.8	0.3	9.8	71	1	1.4	0.0	7.6
	Related	71	13	18.3	10.1	29.3	71	14	19.7	11.2	30.9
Shivering	Any	71	4	5.6	1.6	13.8	71	8	11.3	5.0	21.0
	Grade 3	71	1	1.4	0.0	7.6	71	0	0.0	0.0	5.1
	Related	71	4	5.6	1.6	13.8	71	4	5.6	1.6	13.8
Sweating	Any	71	4	5.6	1.6	13.8	71	7	9.9	4.1	19.3
	Grade 3	71	1	1.4	0.0	7.6	71	0	0.0	0.0	5.1
	Related	71	3	4.2	0.9	11.9	71	3	4.2	0.9	11.9
Temperature/(Axillary) (°C)	≥ 38°C	71	0	0.0	0.0	5.1	71	1	1.4	0.0	7.6
	≥ 39°C	71	0	0.0	0.0	5.1	71	0	0.0	0.0	5.1

	Related	71	0	0.0	0.0	5.1	71	0	0.0	0.0	5.1
Any = occurrence of any general symptom regardless of intensity grade and relationship to vaccination Grade 3 = event that prevented normal activities Related = general symptom assessed by the investigator as causally related to the study vaccination N= number of subjects with the 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): Number of days with any general symptoms during the solicited post-vaccination period of Placebo or Flu S (Total Vaccinated Cohort)											
Solicited symptom	Dose	Group	N	Mean	Min	Q1	Median	Q3	Max		
Fatigue	Dose 1	Group A	9	2.0	1.0	1.0	1.0	2.0	5.0		
		Group B	7	2.1	1.0	1.0	1.0	2.0	7.0		
Headache	Dose 1	Group A	5	2.6	1.0	1.0	2.0	4.0	5.0		
		Group B	10	1.7	1.0	1.0	1.0	2.0	4.0		
Joint pain at other location	Dose 1	Group A	7	3.6	2.0	2.0	3.0	4.0	7.0		
		Group B	2	4.5	4.0	4.0	4.5	5.0	5.0		
Muscle aches	Dose 1	Group A	4	1.8	1.0	1.0	1.5	2.5	3.0		
		Group B	6	2.3	1.0	1.0	1.5	4.0	5.0		
Sweating	Dose 1	Group A	5	2.4	1.0	1.0	1.0	2.0	7.0		
		Group B	6	3.5	1.0	1.0	3.5	5.0	7.0		
Shivering	Dose 1	Group A	2	4.5	2.0	2.0	4.5	7.0	7.0		
		Group B	4	2.3	1.0	1.5	2.5	3.0	3.0		
Temperature	Dose 1	Group B	1	3.0	3.0	3.0	3.0	3.0	3.0		
N = number of doses with the symptom Q1 = 25th percentile Q3 = 75th percentile											
Secondary Outcome Variable(s): Number of days with any general symptoms during the solicited post-vaccination period following first dose of H1N1 candidate vaccine (Total Vaccinated Cohort)											
Solicited symptom	Dose	Group	N	Mean	Min	Q1	Median	Q3	Max		
Fatigue	Dose 2	Group A	13	2.4	1.0	1.0	2.0	3.0	7.0		
		Group B	10	2.6	1.0	1.0	2.0	4.0	7.0		
Headache	Dose 2	Group A	14	2.4	1.0	1.0	2.0	3.0	7.0		
		Group B	9	2.6	1.0	1.0	2.0	2.0	7.0		
Joint pain at other location	Dose 2	Group A	11	3.5	1.0	2.0	3.0	5.0	7.0		
		Group B	4	2.5	1.0	1.5	2.5	3.5	4.0		
Muscle aches	Dose 2	Group A	15	2.9	1.0	2.0	3.0	4.0	7.0		
		Group B	15	2.5	1.0	1.0	2.0	4.0	6.0		
Sweating	Dose 2	Group A	4	1.3	1.0	1.0	1.0	1.5	2.0		
		Group B	7	1.7	1.0	1.0	2.0	2.0	3.0		
Shivering	Dose 2	Group A	4	2.0	1.0	1.0	1.5	3.0	4.0		
		Group B	8	1.6	1.0	1.0	1.5	2.0	3.0		
Temperature	Dose 2	Group B	1	2.0	2.0	2.0	2.0	2.0	2.0		
N = number of doses with the symptom Q1 = 25th percentile Q3 = 75th percentile											
Secondary Outcome Variable(s): Percentage of subjects reporting the occurrence of AEs of specific interest up to Day 21 (Total vaccinated cohort)											
Most frequent AEs of specific interest					Group A N = 72			Group B N = 73			
Subjects with any AE(s) of specific interest, n (%)					0 (0.0)			0 (0.0)			
Safety results: Percentage of subjects reporting the occurrence of unsolicited AEs within the 21-day (Days 0-20) post-vaccination period (Total vaccinated cohort)											
Most frequent adverse events - On-Therapy (occurring within Day 0-20 following vaccination)					Group A N = 72			Group B N = 73			
Subjects with any AE(s), n (%)					23 (31.9)			27 (37.0)			

Nasopharyngitis	9 (12.5)	5 (6.8)
Abdominal pain upper	1 (1.4)	2 (2.7)
Cough	2 (2.8)	1 (1.4)
Diarrhoea	1 (1.4)	2 (2.7)
Cystitis	-	2 (2.7)
Arthralgia	1 (1.4)	-
Back pain	-	1 (1.4)
Blood glucose decreased	1 (1.4)	-
Bronchitis	-	1 (1.4)
Contusion	1 (1.4)	-
Dementia	-	1 (1.4)
Dental prosthesis user	1 (1.4)	-
Dysphonia	1 (1.4)	-
Fatigue	1 (1.4)	-
Gastroenteritis	-	1 (1.4)
Gastrointestinal infection	-	1 (1.4)
Gingivitis	-	1 (1.4)
Headache	1 (1.4)	-
Hyperhidrosis	1 (1.4)	-
Hypertension	-	1 (1.4)
Hypertensive crisis	-	1 (1.4)
Injection site pruritus	1 (1.4)	-
Lumbar vertebral fracture	1 (1.4)	-
Myalgia	-	1 (1.4)
Osteoarthritis	-	1 (1.4)
Pain in extremity	-	1 (1.4)
Palpitations	1 (1.4)	-
Peripheral coldness	1 (1.4)	-
Pneumonia	-	1 (1.4)
Pruritus	1 (1.4)	-
Radius fracture	1 (1.4)	-
Rhinitis	-	1 (1.4)
Rhinorrhoea	-	1 (1.4)
Spinal compression fracture	-	1 (1.4)
Thrombophlebitis	1 (1.4)	-
Tinea pedis	1 (1.4)	-
Tooth disorder	1 (1.4)	-
Visual impairment	-	1 (1.4)

- : Adverse event absent

Safety results: Number (%) of subjects with SAEs up to Day 21 (Total vaccinated cohort)

Serious adverse event, n (%) [n considered by the investigator to be related to study medication]

All SAEs	Group A N = 72	Group B N = 73
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	2 (2.8) [0]	2 (2.7) [1]
Lumbar vertebral fracture	1 (1.4) [0]	0 (0.0) [0]
Myalgia	0 (0.0) [0]	1 (1.4) [1]
Radius fracture	1 (1.4) [0]	0 (0.0) [0]
Spinal compression fracture	0 (0.0) [0]	1 (1.4) [0]
Fatal SAEs	Group A N = 72	Group B N = 73
Subjects with fatal SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]

Conclusion:

At 21 days after the first dose of H1N1 vaccine, administered in subjects aged 61 years and older, all CHMP criteria for

vaccine homologous virus HI antibody response were met in both Group A and Group B, irrespective of the previous administration of Flu vaccine.

Up to Day 21, 23 (31.9%) subjects in Group A and 27 (37.0%) subjects in Group B reported at least one unsolicited AE. Two SAEs were reported in both Group A and B. One of the SAEs reported in Group B, myalgia was assessed by investigator as related to study vaccination. No fatal SAEs were reported up to Day 21.

Publications: None

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