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<b>Study No.:</b> 113535 (Flu D-Pan-H1N1-017)
<b>Title:</b> Immunological equivalence between GSK2340272A and GSK2340274A influenza vaccines in adults aged 18 to 60 years. GSK2340272A (Flu1): GlaxoSmithKline (GSK) Biologicals' Pandemic influenza vaccine comprising A/California/7/2009 (H1N1)v-like strain (manufactured in Dresden) with AS03A adjuvant. GSK2340274A (Flu2): GSK Biologicals' Pandemic influenza vaccine comprising A/California/7/2009 (H1N1)v-like strain (manufactured in Quebec) with AS03A adjuvant.
<b>Rationale:</b> The present study was designed to assess equivalence of immunogenicity between Flu1 and Flu2 vaccines. 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.
<b>Phase:</b> III
<b>Study Period:</b> From 12 October 2009 to 18 November 2009 (data lock point Day 21)
<b>Study Design:</b> Observer-blind, randomised study with two parallel groups.
<b>Centres:</b> 7 centres (4 in France and 3 in Germany).
<b>Indication:</b> Immunization against A/California/7/2009 (H1N1)v-like influenza in male and female subjects aged 18 to 60 years.
<b>Treatment:</b> Study groups were as follows <ul style="list-style-type: none"> <li>Flu1 Group: Subjects received two doses of Flu1 vaccine at Day 0 and Day 21.#</li> <li>Flu2 Group: Subjects received two doses of Flu2 vaccine at Day 0 and Day 21.</li> </ul> Vaccines were administered intramuscularly in the deltoid region of the non-dominant (Day 0) or dominant (Day 21) arm. # Results for Flu1 Group were not available at the time of writing this summary.
<b>Objectives:</b> To assess the immunological equivalence (in terms of vaccine-homologous virus H1N1 HI antibody geometric mean titres [GMTs]) of Flu1 and Flu2 vaccines, 21 days after the first vaccination in healthy subjects aged 18 to 60 years. <i>Criterion for equivalence:</i> <i>Immunological equivalence was demonstrated if the limits of two-sided 95% confidence interval for the GMT ratio (Flu1 vaccine over Flu2 vaccine) in terms of HI antibody titre against A/California/7/2009 (H1N1)v-like strain were within the 0.5 - 2.0 interval.</i> The results presented in this summary were generated by an external statistician who performed an unplanned interim analysis in order to provide Public Health Authorities with the earliest possible data regarding the immunogenicity of Flu2 vaccine. The integrity of the study blind has been maintained.
<b>Primary Outcome/Efficacy Variable:</b> <ul style="list-style-type: none"> <li>Humoral immune response in terms of Haemagglutination Inhibition (HI) antibodies, in all subjects from both groups# against A/California/7/2009 (H1N1)v-like antigen: <ul style="list-style-type: none"> <li>- GMTs 21 days after the first dose of vaccine (Day 21).</li> </ul> </li> </ul> # Results for Flu2 Group only are presented in this summary.
<b>Secondary Outcome/Efficacy Variable(s):</b> <i>Immunogenicity</i> <ul style="list-style-type: none"> <li>Humoral immune response in terms of HI antibodies, in all subjects from both groups# against A/California/7/2009 (H1N1)v-like antigen: <ul style="list-style-type: none"> <li>- GMTs and seropositivity rates at Days 0, 21, 42<sup>§</sup>, 182<sup>§</sup> and 364<sup>§</sup></li> <li>- Seroconversion rate (SCR)* at Days 21, 42<sup>§</sup>, 182<sup>§</sup> and 364<sup>§</sup></li> <li>- Seroprotection rate (SPR)** at Days 0, 21, 42<sup>§</sup>, 182<sup>§</sup> and 364<sup>§</sup></li> <li>- Geometric mean fold rise (GMFR)*** at Days 21, 42<sup>§</sup>, 182<sup>§</sup> and 364<sup>§</sup></li> </ul> </li> </ul> *SCR was defined as the percentage of vaccinees that have either a pre- vaccination titre < 1:10 and a postvaccination titre ≥ 1:40 or a pre vaccination titre ≥ 1:10 and at least a four-fold increase in post-vaccination titre. **SPR was defined as the percentage of vaccinees with a serum HI titre ≥ 1:40, that usually is accepted as indicating protection. ***GMFR (also called seroconversion factor [SCF]) was defined the fold increase in serum HI GMTs post-vaccination compared to pre-vaccination. <ul style="list-style-type: none"> <li>Humoral immune response in terms of neutralizing antibodies, in all subjects from both groups against</li> </ul>

A/California/7/2009 (H1N1)v-like antigen: §

- GMTs at Days 0 and 21

- SCR\* at Day 21

\*SCR was defined as the percentage of vaccinees that have a four-fold increase between pre- and postvaccination titres.

**Safety§**

- Occurrence, duration and intensity of each solicited local adverse event (AE) during the 7-day follow-up period (i.e. day of vaccination and 6 subsequent days) after each vaccination.
- Occurrence, duration, intensity and relation to vaccination of each solicited general AE during the 7-day follow-up period (i.e. day of vaccination and 6 subsequent days) after each vaccination.
- Occurrence, intensity and relationship to vaccination of unsolicited AEs within 21 days after the first vaccination and up to 63 days after the second vaccination (Day 0-Day 20 and Day 21-Day 84), according to the Medical Dictionary for Regulatory Activities (MedDRA) classification.
- Occurrence and relationship to vaccination of adverse events of specific interest (AESIs)/ potential immune-mediated diseases (pIMDs) during the entire study period (up to Day 364).
- Occurrence and relationship to vaccination of serious adverse events (SAEs) during the entire study period (up to Day 364).

§Not available at the time of writing this summary.

# Results for Flu2 Group only are presented in this summary.

**Statistical Methods:**

The analyses were performed on the Total Vaccinated cohort.

- The Total Vaccinated cohort included all vaccinated subjects.

**Immunogenicity:**

The analysis was based on the Total Vaccinated cohort.

For the humoral response in terms of H1N1 HI antibodies in the Flu2 Group, the following parameters (with 95% confidence intervals [CI]) were calculated:

- GMTs of antibodies against vaccine homologous virus at Days 0 and 21.
- Seropositivity rates of antibodies against vaccine homologous virus at Days 0 and 21.
- SCR of antibodies against vaccine homologous virus at Day 21.
- SCF of H1N1 HI antibodies against vaccine homologous virus at Day 21.
- SPR of H1N1 HI antibodies against vaccine homologous virus at Days 0 and 21.

**Study Population:** Healthy male or female adults 18 to 60 years of age at the time of first vaccination, inclusive. Written informed consent was obtained from the subjects prior to study entry.

<b>Number of Subjects:</b>		<b>Flu2 Group</b>
Planned, N		160
Randomised, N (Total Vaccinated cohort)		167
Completed, n (%)		Not available
Total Number Subjects Withdrawn, n (%)		Not available
Withdrawn due to Adverse Events n (%)		Not available
Withdrawn due to Lack of Efficacy n (%)		Not applicable
Withdrawn for other reasons n (%)		Not available
<b>Demographics</b>		<b>Flu2 Group</b>
N (Total Vaccinated cohort)		167
Females: Males		77: 90
Mean Age, years (SD)		39.7 (11.98)
White - Caucasian / European heritage, n (%)		161 (96.4)

**Primary Efficacy Results:** Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/09.HA1 Ab by pre-vaccination status (Total Vaccinated cohort)

Antibody	Group	Pre-vacc status	Timing	N	≥ 10 1/DIL				GMT		
					n	%	95% CI		value	95% CI	
							LL	UL		LL	UL
Flu A/CAL/7/09.HA1 Ab	Flu2	S-	PRE	95	0	0.0	0.0	3.8	5.00	5.00	5.00
			PI(D21)	95	95	100	96.2	100	251.50	203.12	311.39
		S+	PRE	72	72	100	95.0	100	27.41	22.27	33.75
			PI(D21)	71	71	100	94.9	100	484.49	380.45	616.97
		Total	PRE	167	72	43.1	35.5	51.0	10.41	8.90	12.18

			PI(D21)	166	166	100	97.8	100	332.91	281.96	393.06
<p>S- = seronegative subjects (antibody titre &lt; 10 1/DIL) prior to vaccination  S+ = seropositive subjects (antibody titre ≥ 10 1/DIL) 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 titre within the specified range  95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit  PRE = Prevaccination (Day 0)  PI(D21) = Post dose 1 (Day 21)</p>											
<b>Secondary Outcome Variable(s):</b> SCRs for HI antibodies against Flu A/CAL/7/09.HA1 Ab at Day 21 (Total Vaccinated cohort)											
								<b>SCR</b>			
								<b>95% CI</b>			
Strain	Group	Sub-group	Timing	N	n	%	LL	UL			
Flu A/CAL/7/09.HA1 Ab	Flu2	S-	PI(D21)	95	92	96.8	91.0	99.3			
		S+	PI(D21)	71	64	90.1	80.7	95.9			
		Total	PI(D21)	166	156	94.0	89.2	97.1			
<p>S- = seronegative subjects (antibody titre &lt; 10 1/DIL) prior to vaccination  S+ = seropositive subjects (antibody titre ≥ 10 1/DIL) prior to vaccination  Seroconversion defined as:  For initially seronegative subjects, antibody titre ≥ 40 1/DIL 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(D21)= Post dose 1 (Day 21)</p>											
<b>Secondary Outcome Variable(s):</b> SPRs for HI antibodies against Flu A/CAL/7/09.HA1 Ab at Day 0 and Day 21 (Total Vaccinated cohort)											
								<b>SPR</b>			
								<b>95% CI</b>			
Strain	Group	Pre-vacc status	Timing	N	n	%	LL	UL			
Flu A/CAL/7/09.HA1 Ab	Flu2	S-	PRE	95	0	0.0	0.0	3.8			
			PI(D21)	95	92	96.8	91.0	99.3			
		S+	PRE	72	22	30.6	20.2	42.5			
			PI(D21)	71	70	98.6	92.4	100			
		Total	PRE	167	22	13.2	8.4	19.3			
			PI(D21)	166	162	97.6	93.9	99.3			
<p>N = Number of subjects with available results  n (%) = Number (percentage) of seroprotected subjects (HI titre ≥ 40 1/DIL)  95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit  PRE= Prevaccination (Day 0)  PI(D21)= Post dose 1 (Day 21)</p>											
<b>Secondary Outcome Variable(s):</b> SCFs for HI antibody titres at Day 21 (Total Vaccinated cohort)											
								<b>SCF</b>			
								<b>95% CI</b>			
Vaccine strain	Group	Sub-group	Timing	N	Value	LL	UL				
Flu A/CAL/7/09.HA1 Ab (1/DIL)	Flu2	S-	PI(D21)	95	50.3	40.6	62.3				
		S+	PI(D21)	71	17.7	13.3	23.4				
		Total	PI(D21)	166	32.2	26.7	38.8				
<p>S- = seronegative subjects (antibody titre &lt; 10 1/DIL) prior to vaccination  S+ = seropositive subjects (antibody titre ≥ 10 1/DIL) prior to vaccination  N = Number of subjects with pre- and post-vaccination results available  SCF = Seroconversion Factor or geometric mean ratio (mean[log10(POST/PRE)])  95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit  PI(D21)= Post dose 1 (Day 21)</p>											

**Safety Results:** Not available

**Conclusion:**

21 days after the first dose of Flu2 vaccine (Day 21), GMT value for HI antibodies against Flu A/CAL/7/09.HA1 Ab in Flu2 Group was 332.91.

**Publications:** None

Date updated: 15 December 2009