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Study No.: 110464 (Flu Q-PAN-002)
Title: A trial to evaluate the safety and immunogenicity of a two-dose series of monovalent A/Indonesia/5/05 (H5N1) vaccine antigen in association with AS03 adjuvant in adults aged ≥ 18 years.
Rationale: The current trial was performed to evaluate the safety and immunogenicity of 3 consecutive egg-based pandemic influenza (H5N1) antigen lots combined with 3 consecutive lots of adjuvant in pursuit of accelerated approval of the candidate vaccine based on immunologic outcome variables as articulated in the Food and Drug Administration (FDA), Center for Biologics Evaluation and Research (CBER), Guidance of May 2007. Flu: GSK Biologicals' pandemic monovalent (H5N1) influenza vaccines with adjuvant
Phase: III
Study Period: 23 January 2008 to 25 November 2009
Study Design: Randomized (3:1), observer-blind, multi-center, placebo-controlled trial
Centers: 40 centers: 30 in the US and 10 in Canada.
Indication: Immunization against influenza disease caused by an influenza A virus with pandemic potential, subtype H5N1, in adults aged ≥ 18 years.
Treatment: The study groups were as follows: <ul style="list-style-type: none"> • Vaccine Group: subjects received 2 doses of Flu vaccine (lot A, B or C) • Placebo Group: subjects received 2 doses of placebo Subjects were stratified according to the age (18 - 49 years, 50 - 64 years or > 64 years) <p>The first dose was administered in the deltoid region of the non-dominant arm. The second dose was administered in the deltoid region of the dominant arm.</p>
Objectives: <ul style="list-style-type: none"> • To demonstrate that H5N1 antigen in association with adjuvant elicited an immune response, measured by post-immunization vaccine-homologous virus Hemagglutination-inhibition (HI) titers that met or exceeded CBER guidance targets for seroconversion rates and proportions of subjects with reciprocal titer ≥ 40 based on post-immunization reciprocal HI titers. This was tested separately for 2 age strata: 18 to 64 years of age and > 64 years of age. <p><i>Criteria for Evaluation:</i> H5N1 seroconversion rate (SCR) was defined as the percentage of subjects who had either a pre-vaccination (Day 0) reciprocal HI titer < 10 and a post-vaccination (Day 42) reciprocal titer ≥ 40, or a pre-vaccination reciprocal HI titer ≥ 10 and at least a 4-fold increase in post-vaccination reciprocal titer against A/Indonesia/5/05 virus 21 days after the second dose of Flu vaccine in both age strata. If the lower limit of the 95% confidence interval (CI) for SCR was $\geq 40\%$ in subjects 18 to 64 years of age, and $\geq 30\%$ in subjects > 64 years of age, then it was concluded that H5N1 antigen in association with adjuvant elicited an immune response, measured by post-immunization vaccine-homologous virus HI titers, that met or exceeded CBER guidance targets for SCR.</p> <p><i>and</i> The proportion of subjects with reciprocal HI titers ≥ 40 against A/Indonesia/5/05 virus 21 days after the second dose of H5N1 vaccine (abbreviated seroprotection rate [SPR]) in both age strata. That was, if the lower limit of the 95% CI for SPR was $\geq 70\%$ in subjects 18 to 64 years of age, and $\geq 60\%$ in subjects > 64 years of age, then it was concluded that H5N1 antigen in association with the adjuvant elicited an immune response, measured by post-immunization vaccine-homologous virus HI titers, that met or exceeded CBER guidance targets SPR.</p> <ul style="list-style-type: none"> • To demonstrate the immunogenic equivalence, based on vaccine-homologous virus HI geometric mean titers (GMTs), of 3 consecutive lots of Flu vaccine antigen (lot A, B, or C) combined with 3 consecutive lots of adjuvant. The lot consistency hypothesis was addressed in healthy younger adults 18 to 49 years of age. <p><i>Criterion for Evaluation:</i> Equivalence was tested for each of the pair wise ratios of GMT values for A/Indonesia/5/05 reciprocal HI titers formed by the 3 treatment groups representing the 3 consecutive lots. The criterion for success was that the 2-sided 95% confidence bounds for all the ratios were entirely within the interval 0.67 to 1.5.</p> <ul style="list-style-type: none"> • To describe the safety of Flu vaccine antigen with adjuvant in terms of solicited local and general symptoms, unsolicited adverse events (AEs), and serious adverse events (SAEs) in comparison to placebo in adult subjects ≥ 18 years of age.

Primary Outcome/Efficacy Variable:

The primary safety outcome variables were based on:

- The occurrence of specifically-solicited local and general signs and symptoms during a 7-day (Day 0-6) follow-up period after each vaccine administration, and overall per subject considering both post-immunization periods.
- The occurrence of all unsolicited AEs during a 21-day (Day 0-20) follow-up period for each vaccine administration, as well as overall (Day 0-84).
- The occurrence of SAEs and medically-attended events from Day 0 through 364*

* Unsolicited MAEs and SAEs were collected through Day 379 (the limit of the contact window for Day 364 was through Day 379).

The primary immunogenicity outcome variable was based on:

- Vaccine-homologous virus antibody response in subjects receiving 2 doses of study vaccine, as demonstrated by the HI antibody titer at 21 days after the second dose of vaccine for younger adults age 18 to 64 years and older adults age > 64 years (FDA analysis strata for age).

Secondary Outcome/Efficacy Variables:

The secondary and/or exploratory immunogenicity outcome variables were based on:

- Vaccine-homologous virus antibody response in subjects receiving 2 doses of study vaccine, as demonstrated by the HI antibody titer at 21 days after the second dose of Flu vaccine for younger adults (18 to 60 years) and older adults (> 60 years) (European Medicines Agency analysis strata for age).
- Vaccine-homologous virus antibody response in subjects receiving 2 doses of Flu vaccine, as demonstrated by the HI antibody titer at 6 months after the first dose of Flu vaccine for younger adults (18 to 64 years) and older adults (> 64 years).
- Vaccine-homologous virus and drift variant H5N1 virus antibody responses, as assessed by microneutralization assays, in subjects receiving 2 doses of Flu vaccine. The drift-variant viruses currently available are a Clade 1 virus (A/Vietnam/1194/04), a Clade 2, subclade 2 virus (A/turkey/Turkey/1/05), and a Clade 2, subclade 3 virus (A/Anhui/1/05); if available, responses to other recent H5N1 isolates might have also been tested.

Statistical Methods:

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

- The Total Vaccinated Cohort included all subjects who received at least one dose of vaccine for whom any post-vaccination 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) and for whom a complete set of data concerning immunogenicity outcome variables required for the primary outcome variables were available. This implied that all subjects in the ATP for immunogenicity cohort must have had at least Day 0 and 42 HI titer results for the A/Indonesia/5/05 virus. Accordingly, subjects could only be members of the ATP for immunogenicity cohort if they had been randomly selected for immunologic testing and had results. Subjects who received the wrong vaccine were to be excluded from the ATP for immunogenicity cohort. The criteria for exclusion of subjects from the ATP for immunogenicity cohort was established before breaking the blind, and based on the Sponsor's blinded review of protocol violations.

Analysis of Immunogenicity:

The analysis was performed on the ATP cohort for immunogenicity.

The SCR and SPR 21 days after the second dose of the H5N1 vaccine with their two-sided 95% CI were calculated for each major age strata (18 - 64 years and > 64 years). The GMT ratio and the two-sided 95% CI of vaccine-homologous virus reciprocal HI titers at 21 days after the second dose of H5N1 vaccine, in subjects who received 2 doses of vaccine was calculated. The SPR, SCR, and geometric mean fold-rise (GMFR) with their two-sided CI were calculated for the two age strata (18 - 64 years and > 64 years) 21 days after the second vaccination and at 6 months after the first dose. Microneutralization assay titers specific for the vaccine-homologous virus and for one drift-variant virus were determined.

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 7 days (Day 0-6) solicited follow-up period was tabulated with their 95% CI by group and for each age stratum (18 - 64 years and > 64 years). The percentage of subjects with at least one report of unsolicited adverse events classified by the Medical Dictionary for Regulatory Activities (MedDRA) preferred terms and reported up to 21 days (Day 0-20) following each vaccination and up to 85 days (Day 0-84) following initial vaccination were tabulated by group and for each age stratum. The occurrence of SAEs and medically-attended events up to 380 days (Day 0-379) were tabulated by group and for each

age stratum according to MedDRA preferred terms.																			
Study Population: Healthy male or female aged ≥ 18 years at the time of first vaccination. A written informed consent was obtained from the subjects prior to study entry.																			
		18-64 years					> 64 years												
Number of Subjects:		Vaccine Group		Placebo Group			Vaccine Group		Placebo Group										
Planned, N		2220		740			1110		370										
Randomized, N (Total Vaccinated Cohort)		2304		768			1118		371										
Completed, n (%)		2242 (97.3)		750 (97.7)			1101 (98.5)		364 (98.1)										
Total Number Subjects Withdrawn, n (%)		62 (2.7)		18 (2.3)			17 (1.5)		7 (1.9)										
Withdrawn due to Adverse Events n (%)		6 (0.3)		3 (0.4)			2 (0.2)		2 (0.5)										
Withdrawn due to Lack of Efficacy n (%)		Not Applicable		Not Applicable			Not Applicable		Not Applicable										
Withdrawn for other reasons n (%)		56 (2.4)		15 (2.0)			15 (1.3)		5 (1.4)										
Demographics		Vaccine Group		Placebo Group			Vaccine Group		Placebo Group										
N (Total Vaccinated Cohort)		2304		768			1118		371										
Females: Males		1328:976		424:344			621:497		196:175										
Mean Age, years (SD)		38.5 (13.64)		38.7 (13.58)			71.9 (5.49)		72.1 (5.41)										
White – Caucasian/European heritage, n (%)		1980 (85.9)		647 (84.2)			1050 (93.9)		345 (93.0)										
Primary Efficacy Results: A/Indonesia/5/05 SCR at Day 42 in subjects between 18 and 64 years of age and greater than 64 years of age (ATP cohort for immunogenicity)																			
		18-64 years					> 64 years												
				95% CI					95% CI										
Group	Pre-vaccination status	N	n	%	LL	UL	N	n	%	LL	UL								
Vaccine Group	S-	1566	1422	90.8	89.3	92.2	387	287	74.2	69.5	78.5								
	S+	5	5	100	47.8	100	9	6	66.7	29.9	92.5								
	Total	1571	1427	90.8	89.3	92.2	396	293	74.0	69.4	78.2								
Placebo Group	S-	76	1	1.3	0.0	7.1	40	1	2.5	0.1	13.2								
	S+	0	0	-	-	-	0	0	-	-	-								
	Total	76	1	1.3	0.0	7.1	40	1	2.5	0.1	13.2								
S- = seronegative subjects (antibody titer < 1:10 for FLU A/IND/05 AB) prior to vaccination																			
S+ = seropositive subjects (antibody titer $\geq 1:10$ for FLU A/IND/05 AB) prior to vaccination																			
Total = subjects either seropositive or seronegative at pre-vaccination																			
Seroconversion defined as:																			
For initially seronegative subjects, antibody titer $\geq 1:40$ at Day 42																			
For initially seropositive subjects: antibody titer at Day 42 ≥ 4 -fold the pre-vaccination antibody titer																			
N = number of subjects with both pre- and post-vaccination results available																			
n (%) = number (percentage) of responders																			
95% CI = exact 95% confidence interval; LL = lower limit, UL = upper limit																			
Day 42 = 42 days post Dose 1																			
Primary Efficacy Results: Proportion of subjects with post-immunization reciprocal HI antibody titer ≥ 40 (SPR) for A/Indonesia/5/05 antibody at Day 42 for subjects between 18 and 64 years of age and for subjects greater than 64 years of age (ATP cohort for immunogenicity)																			
Group	Timing	18 to 64 years								> 64 years									
		N	$\geq 1:10$			$\geq 1:40$			N	$\geq 1:10$			$\geq 1:40$						
			n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI		
					LL	UL			LL	UL			LL	UL			LL	UL	
Vaccine Group	PRE	1571	5	0.3	0.1	0.7	0	0.0	0.0	0.2	396	9	2.3	1.0	4.3	2	0.5	0.1	1.8
	Day 42	1571	1467	93.4	92.0	94.6	1427	90.8	89.3	92.2	396	334	84.3	80.4	87.8	295	74.5	69.9	78.7
Placebo Group	PRE	76	0	0.0	0.0	4.7	0	0.0	0.0	4.7	40	0	0.0	0.0	8.8	0	0.0	0.0	8.8
	Day 42	76	1	1.3	0.0	7.1	1	1.3	0.0	7.1	40	1	2.5	0.1	13.2	1	2.5	0.1	13.2
N = number of subjects with available results																			
n (%) = number (percentage) of subjects with titer within the specified range																			
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit																			
PRE = Blood sample taken before vaccination																			

Day 42= 42 days post Dose 1											
Primary Efficacy Results: Adjusted ratios of H5N1 GMTs for Lot A and Lot B, Lot A and Lot C, and Lot B and Lot C at Day 42 in subjects between 18 and 49 years of age (ATP cohort for immunogenicity)											
Adjusted GMT	Vaccine Group (Lot A)			Vaccine Group (Lot B)			Vaccine Group (Lot C)				
	N	GMT		N	GMT		N	GMT		LL	UL
	394	275.8		379	291.7		394	333.5			
Adjusted GMT Ratio (95% CI)											
Lot A and Lot B			0.95 (0.78, 1.15)								
Lot A and Lot C			0.83 (0.68, 1.00)								
Lot B and Lot C			0.87 (0.72, 1.06)								
Adjusted GMT = geometric mean antibody titer adjusted for baseline titer											
N = Number of subjects with both pre- and post-vaccination results available											
95% CI = 95% confidence interval for the adjusted GMT ratio; LL = lower limit, UL = upper limit											
Primary Efficacy Results: Incidence of solicited local symptoms reported during the 7-day (Day 0-6) post-vaccination period following each dose and overall (Total Vaccinated cohort)											
Symptom	Intensity	Vaccine Group					Placebo Group				
		N	n	%	95 % CI		N	n	%	95 % CI	
					LL	UL				LL	UL
Dose 1											
Pain	Any	3372	2570	76.2	74.7	77.6	1118	155	13.9	11.9	16.0
	Grade 3	3372	96	2.8	2.3	3.5	1118	3	0.3	0.1	0.8
Redness	>20 mm	3372	180	5.3	4.6	6.2	1118	4	0.4	0.1	0.9
	>100 mm	3372	1	0.0	0.0	0.2	1118	0	0.0	0.0	0.3
Swelling	>20 mm	3372	238	7.1	6.2	8.0	1118	5	0.4	0.1	1.0
	>100 mm	3372	1	0.0	0.0	0.2	1118	0	0.0	0.0	0.3
Dose 2											
Pain	Any	3275	2286	69.8	68.2	71.4	1091	111	10.2	8.4	12.1
	Grade 3	3275	81	2.5	2.0	3.1	1091	5	0.5	0.1	1.1
Redness	>20 mm	3275	163	5.0	4.3	5.8	1091	4	0.4	0.1	0.9
	>100 mm	3275	3	0.1	0.0	0.3	1091	0	0.0	0.0	0.3
Swelling	>20 mm	3275	210	6.4	5.6	7.3	1091	3	0.3	0.1	0.8
	>100 mm	3275	3	0.1	0.0	0.3	1091	0	0.0	0.0	0.3
Across doses											
Pain	Any	3376	2808	83.2	81.9	84.4	1122	224	20.0	17.7	22.4
	Grade 3	3376	156	4.6	3.9	5.4	1122	8	0.7	0.3	1.4
Redness	>20 mm	3376	287	8.5	7.6	9.5	1122	8	0.7	0.3	1.4
	>100 mm	3376	4	0.1	0.0	0.3	1122	0	0.0	0.0	0.3
Swelling	>20 mm	3376	351	10.4	9.4	11.5	1122	8	0.7	0.3	1.4
	>100 mm	3376	4	0.1	0.0	0.3	1122	0	0.0	0.0	0.3
Any = occurrence of any solicited local symptom regardless of their intensity grade											
Grade 3 pain = significant pain at rest; prevented normal activities as assessed by inability to attend/do work or school											
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											
Primary Efficacy Results: Incidence of solicited local symptoms reported during the 7-day (Day 0-6 post-vaccination period following each dose and overall in subjects between 18 and 64 years of age (Total Vaccinated cohort)											
Symptom	Intensity	Vaccine Group					Placebo Group				
		N	n	%	95 % CI		N	n	%	95 % CI	
					LL	UL				LL	UL
Dose 1											
Pain	Any	2264	1904	84.1	82.5	85.6	751	125	16.6	14.0	19.5
	Grade 3	2264	87	3.8	3.1	4.7	751	3	0.4	0.1	1.2
Redness	>20 mm	2264	120	5.3	4.4	6.3	751	4	0.5	0.1	1.4
	>100 mm	2264	1	0.0	0.0	0.2	751	0	0.0	0.0	0.5
Swelling	>20 mm	2264	166	7.3	6.3	8.5	751	4	0.5	0.1	1.4

	>100 mm	2264	1	0.0	0.0	0.2	751	0	0.0	0.0	0.5
Dose 2											
Pain	Any	2189	1679	76.7	74.9	78.5	731	83	11.4	9.1	13.9
	Grade 3	2189	73	3.3	2.6	4.2	731	3	0.4	0.1	1.2
Redness	>20 mm	2189	98	4.5	3.6	5.4	731	3	0.4	0.1	1.2
	>100 mm	2189	3	0.1	0.0	0.4	731	0	0.0	0.0	0.5
Swelling	>20 mm	2189	148	6.8	5.7	7.9	731	3	0.4	0.1	1.2
	>100 mm	2189	2	0.1	0.0	0.3	731	0	0.0	0.0	0.5
Across doses											
Pain	Any	2267	2024	89.3	87.9	90.5	754	171	22.7	19.7	25.8
	Grade 3	2267	141	6.2	5.3	7.3	754	6	0.8	0.3	1.7
Redness	>20 mm	2267	181	8.0	6.9	9.2	754	7	0.9	0.4	1.9
	>100 mm	2267	4	0.2	0.0	0.5	754	0	0.0	0.0	0.5
Swelling	>20 mm	2267	241	10.6	9.4	12.0	754	7	0.9	0.4	1.9
	>100 mm	2267	3	0.1	0.0	0.4	754	0	0.0	0.0	0.5
<p>Any = occurrence of any solicited local symptom regardless of their intensity grade Grade 3 pain = significant pain at rest; prevented normal activities as assessed by inability to attend/do work or school 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</p>											
Primary Efficacy Results: Incidence of solicited local symptoms reported during the 7-day (Day 0-6) post-vaccination period following each dose and overall in subjects greater than 64 years of age (Total Vaccinated cohort)											
Symptom	Intensity	Vaccine Group					Placebo Group				
		N	n	%	95 % CI		N	n	%	95 % CI	
					LL	UL				LL	UL
Dose 1											
Pain	Any	1108	666	60.1	57.2	63	367	30	8.2	5.6	11.5
	Grade 3	1108	9	0.8	0.4	1.5	367	0	0.0	0.0	1.0
Redness	>20 mm	1108	60	5.4	4.2	6.9	367	0	0.0	0.0	1.0
	>100 mm	1108	0	0.0	0.0	0.3	367	0	0.0	0.0	1.0
Swelling	>20 mm	1108	72	6.5	5.1	8.1	367	1	0.3	0.0	1.5
	>100 mm	1108	0	0.0	0.0	0.3	367	0	0.0	0.0	1.0
Dose 2											
Pain	Any	1086	607	55.9	52.9	58.9	360	28	7.8	5.2	11
	Grade 3	1086	8	0.7	0.3	1.4	360	2	0.6	0.1	2.0
Redness	>20 mm	1086	65	6.0	4.6	7.6	360	1	0.3	0.0	1.5
	>100 mm	1086	0	0.0	0.0	0.3	360	0	0.0	0.0	1.0
Swelling	>20 mm	1086	62	5.7	4.4	7.3	360	0	0.0	0.0	1.0
	>100 mm	1086	1	0.1	0.0	0.5	360	0	0.0	0.0	1.0
Across doses											
Pain	Any	1109	784	70.7	67.9	73.4	368	53	14.4	11	18.4
	Grade 3	1109	15	1.4	0.8	2.2	368	2	0.5	0.1	1.9
Redness	>20 mm	1109	106	9.6	7.9	11.4	368	1	0.3	0.0	1.5
	>100 mm	1109	0	0.0	0.0	0.3	368	0	0.0	0.0	1.0
Swelling	>20 mm	1109	110	9.9	8.2	11.8	368	1	0.3	0.0	1.5
	>100 mm	1109	1	0.1	0.0	0.5	368	0	0.0	0.0	1.0
<p>Any = occurrence of any solicited local symptom regardless of their intensity grade Grade 3 pain = significant pain at rest; prevented normal activities as assessed by inability to attend/do work or school 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</p>											
Primary Efficacy Results: Incidence of solicited general symptoms reported during the 7-day (Day 0-6) post-vaccination period following each dose and overall (Total Vaccinated cohort)											
Symptom	Intensity/ Relationship	Vaccine Group				Placebo Group					
		N	n	%	95 % CI	N	n	%	95 % CI		

					LL	UL				LL	UL
Dose 1											
Fatigue	Any	3367	792	23.5	22.1	25.0	1118	198	17.7	15.5	20.1
	Grade 3	3367	52	1.5	1.2	2.0	1118	18	1.6	1.0	2.5
	Related	3367	720	21.4	20.0	22.8	1118	169	15.1	13.1	17.4
Headache	Any	3367	843	25.0	23.6	26.5	1118	245	21.9	19.5	24.5
	Grade 3	3367	40	1.2	0.9	1.6	1118	12	1.1	0.6	1.9
	Related	3367	749	22.2	20.9	23.7	1118	191	17.1	14.9	19.4
Joint pain at other location	Any	3367	548	16.3	15	17.6	1118	98	8.8	7.2	10.6
	Grade 3	3367	31	0.9	0.6	1.3	1118	6	0.5	0.2	1.2
	Related	3367	497	14.8	13.6	16.0	1118	78	7.0	5.6	8.6
Muscle aches	Any	3367	1176	34.9	33.3	36.6	1118	162	14.5	12.5	16.7
	Grade 3	3367	55	1.6	1.2	2.1	1118	10	0.9	0.4	1.6
	Related	3367	1106	32.8	31.3	34.5	1118	136	12.2	10.3	14.2
Shivering	Any	3367	280	8.3	7.4	9.3	1118	82	7.3	5.9	9.0
	Grade 3	3367	20	0.6	0.4	0.9	1118	8	0.7	0.3	1.4
	Related	3367	249	7.4	6.5	8.3	1118	61	5.5	4.2	7.0
Sweating	Any	3367	205	6.1	5.3	6.9	1118	57	5.1	3.9	6.6
	Grade 3	3367	10	0.3	0.1	0.5	1118	6	0.5	0.2	1.2
	Related	3367	182	5.4	4.7	6.2	1118	43	3.8	2.8	5.1
Temperature/(Oral) (°C)	≥38	3367	55	1.6	1.2	2.1	1118	24	2.1	1.4	3.2
	≥39 (=Grade 3)	3367	11	0.3	0.2	0.6	1118	6	0.5	0.2	1.2
	≥39.5	3367	4	0.1	0.0	0.3	1118	4	0.4	0.1	0.9
	Related	3367	40	1.2	0.9	1.6	1118	13	1.2	0.6	2.0
Dose 2											
Fatigue	Any	3272	753	23.0	21.6	24.5	1092	114	10.4	8.7	12.4
	Grade 3	3272	61	1.9	1.4	2.4	1092	8	0.7	0.3	1.4
	Related	3272	699	21.4	20.0	22.8	1092	99	9.1	7.4	10.9
Headache	Any	3272	710	21.7	20.3	23.2	1092	145	13.3	11.3	15.4
	Grade 3	3272	62	1.9	1.5	2.4	1092	17	1.6	0.9	2.5
	Related	3272	641	19.6	18.2	21.0	1092	122	11.2	9.4	13.2
Joint pain at other location	Any	3272	538	16.4	15.2	17.8	1092	65	6.0	4.6	7.5
	Grade 3	3272	35	1.1	0.7	1.5	1092	4	0.4	0.1	0.9
	Related	3272	514	15.7	14.5	17.0	1092	54	4.9	3.7	6.4
Muscle aches	Any	3272	1032	31.5	29.9	33.2	1092	98	9.0	7.3	10.8
	Grade 3	3272	62	1.9	1.5	2.4	1092	11	1.0	0.5	1.8
	Related	3272	981	30.0	28.4	31.6	1092	89	8.2	6.6	9.9
Shivering	Any	3272	373	11.4	10.3	12.5	1092	50	4.6	3.4	6.0
	Grade 3	3272	47	1.4	1.1	1.9	1092	4	0.4	0.1	0.9
	Related	3272	350	10.7	9.7	11.8	1092	40	3.7	2.6	5.0
Sweating	Any	3272	212	6.5	5.7	7.4	1092	40	3.7	2.6	5.0
	Grade 3	3272	19	0.6	0.3	0.9	1092	7	0.6	0.3	1.3
	Related	3272	197	6.0	5.2	6.9	1092	31	2.8	1.9	4.0
Temperature/(Oral) (°C)	≥38	3272	105	3.2	2.6	3.9	1092	17	1.6	0.9	2.5
	≥39 (=Grade 3)	3272	20	0.6	0.4	0.9	1092	4	0.4	0.1	0.9
	≥39.5	3272	7	0.2	0.1	0.4	1092	1	0.1	0.0	0.5
	Related	3272	87	2.7	2.1	3.3	1092	10	0.9	0.4	1.7
Across doses											
Fatigue	Any	3375	1148	34.0	32.4	35.6	1123	253	22.5	20.1	25.1
	Grade 3	3375	107	3.2	2.6	3.8	1123	26	2.3	1.5	3.4
	Related	3375	1065	31.6	30.0	33.2	1123	221	19.7	17.4	22.1
Headache	Any	3375	1179	34.9	33.3	36.6	1123	312	27.8	25.2	30.5
	Grade 3	3375	97	2.9	2.3	3.5	1123	27	2.4	1.6	3.5
	Related	3375	1076	31.9	30.3	33.5	1123	254	22.6	20.2	25.2

Joint pain at other location	Any	3375	853	25.3	23.8	26.8	1123	136	12.1	10.3	14.2
	Grade 3	3375	63	1.9	1.4	2.4	1123	10	0.9	0.4	1.6
	Related	3375	797	23.6	22.2	25.1	1123	112	10.0	8.3	11.9
Muscle aches	Any	3375	1526	45.2	43.5	46.9	1123	231	20.6	18.2	23.1
	Grade 3	3375	109	3.2	2.7	3.9	1123	21	1.9	1.2	2.8
	Related	3375	1457	43.2	41.5	44.9	1123	201	17.9	15.7	20.3
Shivering	Any	3375	563	16.7	15.4	18.0	1123	109	9.7	8.0	11.6
	Grade 3	3375	66	2.0	1.5	2.5	1123	12	1.1	0.6	1.9
	Related	3375	521	15.4	14.2	16.7	1123	84	7.5	6.0	9.2
Sweating	Any	3375	362	10.7	9.7	11.8	1123	82	7.3	5.8	9.0
	Grade 3	3375	28	0.8	0.6	1.2	1123	13	1.2	0.6	2.0
	Related	3375	329	9.7	8.8	10.8	1123	65	5.8	4.5	7.3
Temperature/(Oral) (°C)	≥38	3375	156	4.6	3.9	5.4	1123	38	3.4	2.4	4.6
	≥39 (=Grade 3)	3375	31	0.9	0.6	1.3	1123	10	0.9	0.4	1.6
	≥39.5	3375	11	0.3	0.2	0.6	1123	5	0.4	0.1	1.0
	Related	3375	123	3.6	3.0	4.3	1123	21	1.9	1.2	2.8

Any= occurrence of any solicited general symptom regardless of their intensity grade or relationship to vaccination
Grade 3 headache, fatigue, joint pain at other location, muscle aches, shivering, and sweating = prevented normal everyday activities as assessed by inability to attend/do work or school, or required intervention of a physician/healthcare provider

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

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

Primary Efficacy Results: Incidence of solicited general symptoms reported during the 7-day (Day 0-6) post-vaccination period following each dose and overall in subjects between 18 and 64 years of age (Total Vaccinated cohort)

Symptom	Intensity/ Relationship	Vaccine Group					Placebo Group				
		N	n	%	95 % CI		N	n	%	95 % CI	
					LL	UL				LL	UL
Dose 1											
Fatigue	Any	2261	628	27.8	25.9	29.7	751	151	20.1	17.3	23.2
	Grade 3	2261	44	1.9	1.4	2.6	751	15	2.0	1.1	3.3
	Related	2261	579	25.6	23.8	27.5	751	129	17.2	14.5	20.1
Headache	Any	2261	679	30.0	28.1	32.0	751	198	26.4	23.2	29.7
	Grade 3	2261	36	1.6	1.1	2.2	751	11	1.5	0.7	2.6
	Related	2261	608	26.9	25.1	28.8	751	156	20.8	17.9	23.9
Joint pain at other location	Any	2261	432	19.1	17.5	20.8	751	71	9.5	7.5	11.8
	Grade 3	2261	28	1.2	0.8	1.8	751	5	0.7	0.2	1.5
	Related	2261	396	17.5	16.0	19.1	751	61	8.1	6.3	10.3
Muscle aches	Any	2261	937	41.4	39.4	43.5	751	123	16.4	13.8	19.2
	Grade 3	2261	46	2.0	1.5	2.7	751	7	0.9	0.4	1.9
	Related	2261	881	39.0	36.9	41.0	751	104	13.8	11.5	16.5
Shivering	Any	2261	233	10.3	9.1	11.6	751	66	8.8	6.9	11.0
	Grade 3	2261	15	0.7	0.4	1.1	751	6	0.8	0.3	1.7
	Related	2261	210	9.3	8.1	10.6	751	54	7.2	5.4	9.3
Sweating	Any	2261	182	8.0	7.0	9.2	751	47	6.3	4.6	8.2
	Grade 3	2261	8	0.4	0.2	0.7	751	4	0.5	0.1	1.4
	Related	2261	161	7.1	6.1	8.3	751	37	4.9	3.5	6.7
Temperature/(Oral) (°C)	≥38	2261	40	1.8	1.3	2.4	751	20	2.7	1.6	4.1
	≥39 (=Grade 3)	2261	9	0.4	0.2	0.8	751	6	0.8	0.3	1.7
	≥39.5	2261	3	0.1	0.0	0.4	751	4	0.5	0.1	1.4
	Related	2261	29	1.3	0.9	1.8	751	10	1.3	0.6	2.4
Dose 2											
Fatigue	Any	2188	584	26.7	24.8	28.6	732	84	11.5	9.3	14.0

	Grade 3	2188	51	2.3	1.7	3.1	732	6	0.8	0.3	1.8
	Related	2188	544	24.9	23.1	26.7	732	72	9.8	7.8	12.2
Headache	Any	2188	559	25.5	23.7	27.4	732	118	16.1	13.5	19.0
	Grade 3	2188	57	2.6	2.0	3.4	732	15	2.0	1.2	3.4
	Related	2188	510	23.3	21.6	25.1	732	98	13.4	11.0	16.1
Joint pain at other location	Any	2188	403	18.4	16.8	20.1	732	46	6.3	4.6	8.3
	Grade 3	2188	30	1.4	0.9	2.0	732	3	0.4	0.1	1.2
	Related	2188	390	17.8	16.2	19.5	732	39	5.3	3.8	7.2
Muscle aches	Any	2188	810	37.0	35.0	39.1	732	74	10.1	8.0	12.5
	Grade 3	2188	56	2.6	1.9	3.3	732	10	1.4	0.7	2.5
	Related	2188	774	35.4	33.4	37.4	732	67	9.2	7.2	11.5
Shivering	Any	2188	300	13.7	12.3	15.2	732	39	5.3	3.8	7.2
	Grade 3	2188	44	2.0	1.5	2.7	732	3	0.4	0.1	1.2
	Related	2188	284	13.0	11.6	14.5	732	31	4.2	2.9	6.0
Sweating	Any	2188	184	8.4	7.3	9.7	732	33	4.5	3.1	6.3
	Grade 3	2188	19	0.9	0.5	1.4	732	7	1.0	0.4	2.0
	Related	2188	171	7.8	6.7	9.0	732	25	3.4	2.2	5.0
Temperature/(Oral) (°C)	≥38	2188	85	3.9	3.1	4.8	732	15	2.0	1.2	3.4
	≥39 (=Grade 3)	2188	19	0.9	0.5	1.4	732	4	0.5	0.1	1.4
	≥39.5	2188	6	0.3	0.1	0.6	732	1	0.1	0.0	0.8
	Related	2188	73	3.3	2.6	4.2	732	9	1.2	0.6	2.3
Across doses											
Fatigue	Any	2266	890	39.3	37.3	41.3	755	189	25.0	22.0	28.3
	Grade 3	2266	89	3.9	3.2	4.8	755	21	2.8	1.7	4.2
	Related	2266	829	36.6	34.6	38.6	755	164	21.7	18.8	24.8
Headache	Any	2266	932	41.1	39.1	43.2	755	249	33.0	29.6	36.5
	Grade 3	2266	89	3.9	3.2	4.8	755	24	3.2	2.0	4.7
	Related	2266	856	37.8	35.8	39.8	755	203	26.9	23.8	30.2
Joint pain at other location	Any	2266	645	28.5	26.6	30.4	755	97	12.8	10.5	15.4
	Grade 3	2266	55	2.4	1.8	3.1	755	8	1.1	0.5	2.1
	Related	2266	610	26.9	25.1	28.8	755	84	11.1	9.0	13.6
Muscle aches	Any	2266	1188	52.4	50.3	54.5	755	175	23.2	20.2	26.4
	Grade 3	2266	95	4.2	3.4	5.1	755	17	2.3	1.3	3.6
	Related	2266	1139	50.3	48.2	52.3	755	152	20.1	17.3	23.2
Shivering	Any	2266	456	20.1	18.5	21.8	755	87	11.5	9.3	14.0
	Grade 3	2266	58	2.6	1.9	3.3	755	9	1.2	0.5	2.3
	Related	2266	427	18.8	17.3	20.5	755	70	9.3	7.3	11.6
Sweating	Any	2266	314	13.9	12.5	15.3	755	67	8.9	6.9	11.1
	Grade 3	2266	26	1.1	0.8	1.7	755	11	1.5	0.7	2.6
	Related	2266	285	12.6	11.2	14.0	755	54	7.2	5.4	9.2
Temperature/(Oral)(°C)	≥38	2266	121	5.3	4.5	6.3	755	32	4.2	2.9	5.9
	≥39 (=Grade 3)	2266	28	1.2	0.8	1.8	755	10	1.3	0.6	2.4
	≥39.5	2266	9	0.4	0.2	0.8	755	5	0.7	0.2	1.5
	Related	2266	98	4.3	3.5	5.2	755	17	2.3	1.3	3.6
<p>Any: occurrence of any solicited general symptom regardless of their intensity grade or relationship to vaccination Grade 3 headache, fatigue, joint pain at other location, muscle aches, shivering, and sweating = prevented normal everyday activities as assessed by inability to attend/do work or school, or required intervention of a physician/healthcare provider Related = general symptom assessed by the investigator as causally related to the study vaccination 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</p>											
Primary Efficacy Results: Incidence of solicited general symptoms reported during the 7-day (Day 0-6) post-vaccination period following each dose and overall in subjects greater than 64 years of age (Total Vaccinated cohort)											

		Vaccine Group					Placebo Group				
					95 % CI					95 % CI	
Symptom	Intensity/ Relationship	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1											
Fatigue	Any	1106	164	14.8	12.8	17.1	367	47	12.8	9.6	16.7
	Grade 3	1106	8	0.7	0.3	1.4	367	3	0.8	0.2	2.4
	Related	1106	141	12.7	10.8	14.9	367	40	10.9	7.9	14.5
Headache	Any	1106	164	14.8	12.8	17.1	367	47	12.8	9.6	16.7
	Grade 3	1106	4	0.4	0.1	0.9	367	1	0.3	0.0	1.5
	Related	1106	141	12.7	10.8	14.9	367	35	9.5	6.7	13.0
Joint pain at other location	Any	1106	116	10.5	8.7	12.4	367	27	7.4	4.9	10.5
	Grade 3	1106	3	0.3	0.1	0.8	367	1	0.3	0.0	1.5
	Related	1106	101	9.1	7.5	11.0	367	17	4.6	2.7	7.3
Muscle aches	Any	1106	239	21.6	19.2	24.2	367	39	10.6	7.7	14.2
	Grade 3	1106	9	0.8	0.4	1.5	367	3	0.8	0.2	2.4
	Related	1106	225	20.3	18.0	22.8	367	32	8.7	6.0	12.1
Shivering	Any	1106	47	4.2	3.1	5.6	367	16	4.4	2.5	7.0
	Grade 3	1106	5	0.5	0.1	1.1	367	2	0.5	0.1	2.0
	Related	1106	39	3.5	2.5	4.8	367	7	1.9	0.8	3.9
Sweating	Any	1106	23	2.1	1.3	3.1	367	10	2.7	1.3	5.0
	Grade 3	1106	2	0.2	0.0	0.7	367	2	0.5	0.1	2.0
	Related	1106	21	1.9	1.2	2.9	367	6	1.6	0.6	3.5
Temperature/(Oral) (°C)	≥38	1106	15	1.4	0.8	2.2	367	4	1.1	0.3	2.8
	≥39 (=Gr. 3)	1106	2	0.2	0.0	0.7	367	0	0.0	0.0	1.0
	≥39.5	1106	1	0.1	0.0	0.5	367	0	0.0	0.0	1.0
	Related	1106	11	1.0	0.5	1.8	367	3	0.8	0.2	2.4
Dose 2											
Fatigue	Any	1084	169	15.6	13.5	17.9	360	30	8.3	5.7	11.7
	Grade 3	1084	10	0.9	0.4	1.7	360	2	0.6	0.1	2.0
	Related	1084	155	14.3	12.3	16.5	360	27	7.5	5.0	10.7
Headache	Any	1084	151	13.9	11.9	16.1	360	27	7.5	5.0	10.7
	Grade 3	1084	5	0.5	0.1	1.1	360	2	0.6	0.1	2.0
	Related	1084	131	12.1	10.2	14.2	360	24	6.7	4.3	9.8
Joint pain at other location	Any	1084	135	12.5	10.5	14.6	360	19	5.3	3.2	8.1
	Grade 3	1084	5	0.5	0.1	1.1	360	1	0.3	0.0	1.5
	Related	1084	124	11.4	9.6	13.5	360	15	4.2	2.4	6.8
Muscle aches	Any	1084	222	20.5	18.1	23	360	24	6.7	4.3	9.8
	Grade 3	1084	6	0.6	0.2	1.2	360	1	0.3	0.0	1.5
	Related	1084	207	19.1	16.8	21.6	360	22	6.1	3.9	9.1
Shivering	Any	1084	73	6.7	5.3	8.4	360	11	3.1	1.5	5.4
	Grade 3	1084	3	0.3	0.1	0.8	360	1	0.3	0.0	1.5
	Related	1084	66	6.1	4.7	7.7	360	9	2.5	1.1	4.7
Sweating	Any	1084	28	2.6	1.7	3.7	360	7	1.9	0.8	4.0
	Grade 3	1084	0	0.0	0.0	0.3	360	0	0.0	0.0	1.0
	Related	1084	26	2.4	1.6	3.5	360	6	1.7	0.6	3.6
Temperature/(Oral) (°C)	≥38	1084	20	1.8	1.1	2.8	360	2	0.6	0.1	2.0
	≥39 (=Gr. 3)	1084	1	0.1	0.0	0.5	360	0	0.0	0.0	1.0
	≥39.5	1084	1	0.1	0.0	0.5	360	0	0.0	0.0	1.0
	Related	1084	14	1.3	0.7	2.2	360	1	0.3	0.0	1.5
Across doses											
Fatigue	Any	1109	258	23.3	20.8	25.9	368	64	17.4	13.7	21.7
	Grade 3	1109	18	1.6	1.0	2.6	368	5	1.4	0.4	3.1
	Related	1109	236	21.3	18.9	23.8	368	57	15.5	11.9	19.6

Headache	Any	1109	247	22.3	19.9	24.8	368	63	17.1	13.4	21.4
	Grade 3	1109	8	0.7	0.3	1.4	368	3	0.8	0.2	2.4
	Related	1109	220	19.8	17.5	22.3	368	51	13.9	10.5	17.8
Joint pain at other location	Any	1109	208	18.8	16.5	21.2	368	39	10.6	7.6	14.2
	Grade 3	1109	8	0.7	0.3	1.4	368	2	0.5	0.1	1.9
	Related	1109	187	16.9	14.7	19.2	368	28	7.6	5.1	10.8
Muscle aches	Any	1109	338	30.5	27.8	33.3	368	56	15.2	11.7	19.3
	Grade 3	1109	14	1.3	0.7	2.1	368	4	1.1	0.3	2.8
	Related	1109	318	28.7	26.0	31.4	368	49	13.3	10.0	17.2
Shivering	Any	1109	107	9.6	8.0	11.5	368	22	6.0	3.8	8.9
	Grade 3	1109	8	0.7	0.3	1.4	368	3	0.8	0.2	2.4
	Related	1109	94	8.5	6.9	10.3	368	14	3.8	2.1	6.3
Sweating	Any	1109	48	4.3	3.2	5.7	368	15	4.1	2.3	6.6
	Grade 3	1109	2	0.2	0.0	0.6	368	2	0.5	0.1	1.9
	Related	1109	44	4.0	2.9	5.3	368	11	3.0	1.5	5.3
Temperature/(Oral) (°C)	≥38	1109	35	3.2	2.2	4.4	368	6	1.6	0.6	3.5
	≥39 (=Gr. 3)	1109	3	0.3	0.1	0.8	368	0	0.0	0.0	1.0
	≥39.5	1109	2	0.2	0.0	0.6	368	0	0.0	0.0	1.0
	Related	1109	25	2.3	1.5	3.3	368	4	1.1	0.3	2.8

Any: occurrence of any solicited general symptom regardless of their intensity grade or relationship to vaccination
Grade 3 headache, fatigue, joint pain at other location, muscle aches, shivering, and sweating = prevented normal everyday activities as assessed by inability to attend/do work or school, or required intervention of a physician/healthcare provider

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

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

Primary Efficacy Results: Most frequent medically attended AEs occurring during Days 0-182 in subjects between 18 and 64 years of age (Total Vaccinated cohort)

Most frequent adverse events - On-Therapy (occurring within Day 0-182)	Vaccine Group N = 2304	Placebo Group N = 768
Subjects with any AE(s), n (%)	480 (20.8)	154 (20.1)
Sinusitis	44 (1.9)	9 (1.2)
Upper respiratory tract infection	26 (1.1)	13 (1.7)
Bronchitis	31 (1.3)	7 (0.9)
Urinary tract infection	26 (1.1)	9 (1.2)
Pharyngitis streptococcal	16 (0.7)	4 (0.5)
Depression	17 (0.7)	-
Hypertension	10 (0.4)	5 (0.7)
Cough	9 (0.4)	4 (0.5)
Influenza	9 (0.4)	4 (0.5)
Skin laceration	11 (0.5)	-
Back pain	-	6 (0.8)
Migraine	-	5 (0.7)
Oropharyngeal pain	-	4 (0.5)
Tooth abscess	-	4 (0.5)

- : Event absent or not meeting the selected rule(s): more than 30 subjects per treatment group and ≤ 3 groups: only the 10 most frequent events in each group are to be listed.

Primary Efficacy Results: Most frequent medically attended AEs occurring during Days 0-182 in subjects greater than 64 years of age (Total Vaccinated cohort)

Most frequent adverse events - On-Therapy (occurring within Day 0-182)	Vaccine Group N = 1118	Placebo Group N = 371
Subjects with any AE(s), n (%)	298 (26.7)	92 (24.8)
Bronchitis	18 (1.6)	9 (2.4)
Urinary tract infection	17 (1.5)	4 (1.1)

Hypertension	15 (1.3)	5 (1.3)
Upper respiratory tract infection	13 (1.2)	6 (1.6)
Back pain	10 (0.9)	3 (0.8)
Sinusitis	11 (1.0)	-
Joint sprain	7 (0.6)	3 (0.8)
Pneumonia	8 (0.7)	2 (0.5)
Cough	9 (0.8)	-
Pain in extremity	7 (0.6)	2 (0.5)
Cystitis	7 (0.6)	-
Skin laceration	7 (0.6)	-
Dermatitis contact	-	3 (0.8)
Herpes zoster	-	3 (0.8)
Influenza	-	3 (0.8)
Arthralgia	-	2 (0.5)
Fall	-	2 (0.5)
Gout	-	2 (0.5)
Influenza like illness	-	2 (0.5)
Local swelling	-	2 (0.5)
- : Event absent or not meeting the selected rule(s): more than 30 subjects per treatment group and ≤ 3 groups: only the 10 most frequent events in each group are to be listed.		
Primary Efficacy Results: Most frequent medically attended AEs occurring through Days 0-379* in subjects between 18 and 64 years of age (Total Vaccinated cohort)		
Most frequent adverse events - On-Therapy (occurring within Day 0-379)	Vaccine Group N = 2304	Placebo Group N = 768
Subjects with any AE(s), n (%)	627 (27.2)	212 (27.6)
Sinusitis	58 (2.5)	16 (2.1)
Bronchitis	37 (1.6)	9 (1.2)
Upper respiratory tract infection	36 (1.6)	18 (2.3)
Urinary tract infection	35 (1.5)	10 (1.3)
Depression	22 (1.0)	-
Pharyngitis streptococcal	21 (0.9)	-
Skin laceration	16 (0.7)	-
Hypertension	16 (0.7)	8 (1.0)
Back pain	15 (0.7)	7 (0.9)
Ear infection	11 (0.5)	-
Anxiety	11 (0.5)	7 (0.9)
Gastroesophageal reflux	-	7 (0.9)
Muscle strain	-	5 (0.7)
Migraine	-	5 (0.7)
Cough	-	5 (0.7)
* Unsolicited MAEs were collected through Day 379 (the limit of the contact window for Day 364 was through Day 379). - : Event absent or not meeting the selected rule(s): more than 30 subjects per treatment group and ≤ 3 groups: only the 10 most frequent events in each group are to be listed.		
Primary Efficacy Results: Most frequent medically attended AEs* occurring through Days 0-379 in subjects greater than 64 years of age (Total Vaccinated cohort)		
Most frequent adverse events - On-Therapy (occurring within Day 0-182)	Vaccine Group N = 1118	Placebo Group N = 371
Subjects with any AE(s), n (%)	400 (35.8)	134 (36.1)
Bronchitis	22 (2.0)	11 (3.0)
Urinary tract infection	21 (1.9)	6 (1.6)
Upper respiratory tract infection	18 (1.6)	6 (1.6)
Hypertension	17 (1.5)	9 (2.4)
Sinusitis	15 (1.3)	-
Back pain	14 (1.3)	-

Cough	12 (1.1)	-
Pneumonia	12 (1.1)	-
Rotator cuff syndrome	10 (0.9)	-
Arthralgia	9 (0.8)	4 (1.1)
Osteoarthritis	9 (0.8)	-
Cystitis	9 (0.8)	-
Joint sprain	-	4 (1.1)
Influenza	-	4 (1.1)
Herpes zoster	-	4 (1.1)
Basal cell carcinoma	-	4 (1.1)
Hyperthyroidism	-	4 (1.1)

* Unsolicited MAEs were collected through Day 379 (the limit of the contact window for Day 364 was through Day 379).
- : Event absent or not meeting the selected rule(s); more than 30 subjects per treatment group and ≤ 3 groups: only the 10 most frequent events in each group are to be listed.

Primary Efficacy Results: Occurrence of all unsolicited AEs during a 21-day (Day 0-20) follow-up period for each vaccine administration, as well as overall (Day 0-84); please refer to the safety section at the end of the document.

Primary Efficacy Results: Occurrence of serious adverse events from Day 0 through Day 379; please refer to the safety section at the end of the document.

Secondary Outcome Variables: A/Indonesia/5/05 SCR at Day 42 in subjects between 18 and 60 years of age and in subjects greater than 60 years of age (ATP cohort for immunogenicity)

			18 to 60 years				> 60 years				
			95% CI				95% CI				
Group	Pre-vaccination status	N	n	%	LL	UL	N	n	%	LL	UL
Vaccine Group	S-	1484	1350	91.0	89.4	92.4	469	359	76.5	72.4	80.3
	S+	4	4	100	39.8	100	10	7	70.0	34.8	93.3
	Total	1488	1354	91.0	89.4	92.4	479	366	76.4	72.3	80.1
Placebo Group	S-	68	1	1.5	0.0	7.9	48	1	2.1	0.1	11.1
	S+	0	0	-	-	-	0	0	-	-	-
	Total	68	1	1.5	0.0	7.9	48	1	2.1	0.1	11.1

S- = seronegative subjects (antibody titer < 1:10 for FLU A/IND/05 AB) prior to vaccination

S+ = seropositive subjects (antibody titer ≥ 1:10 for FLU A/IND/05 AB) prior to vaccination

Total = subjects either seropositive or seronegative at pre-vaccination

Seroconversion defined as:

For initially seronegative subjects, antibody titer ≥ 1:40 at Day 42

For initially seropositive subjects: antibody titer at Day 42 ≥ 4-fold the pre-vaccination antibody titer

N = number of subjects with both pre- and post-vaccination results available

n (%) = number (percentage) of responders

95% CI = exact 95% confidence interval; LL = lower limit, UL = upper limit

Day 42 = 42 days post Dose 1

Secondary Outcome Variables: Proportion of subjects with post-immunization reciprocal HI antibody titer ≥ 40 (SPR) for A/Indonesia/5/05 antibodies at Day 42 in subjects between 18 and 60 years of age and in subjects greater than 60 years of age (ATP cohort for immunogenicity)

Group	Timing	18 to 60 years										> 60 years							
		N	≥ 1:10				≥ 1:40				N	≥ 1:10				≥ 1:40			
			n	%	95% CI		n	%	95% CI			n	%	95% CI		n	%	95% CI	
					LL	UL			LL	UL				LL	UL			LL	UL
Vaccine Group	PRE	1488	4	0.3	0.1	0.7	0	0.0	0.0	0.2	479	10	2.1	1.0	3.8	2	0.4	0.1	1.5
	Day 42	1488	1391	93.5	92.1	94.7	1354	91.0	89.4	92.4	479	410	85.6	82.1	88.6	368	76.8	72.8	80.5
Placebo Group	PRE	68	0	0.0	0.0	5.3	0	0.0	0.0	5.3	48	0	0.0	0.0	7.4	0	0.0	0.0	7.4
	Day 42	68	1	1.5	0.0	7.9	1	1.5	0.0	7.9	48	1	2.1	0.1	11.1	1	2.1	0.1	11.1

SPR = Flu A/Indonesia/5/05 antibody titer ≥ 1:40

N = number of subjects with available results

n (%) = number (percentage) of subjects with titer within the specified range

95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit

PRE = Blood sample taken before vaccination							
Day 42 = 42 days post Dose 1							
Secondary Outcome Variables: Vaccine response rate for H5N1 antibodies as assessed by microneutralization assays at Day 42 in subjects between 18 and 64 years of age (ATP cohort for immunogenicity)							
Antibody	Group	Pre-vaccination status	N	Vaccine response			
				n	%	95% CI	
						LL	UL
Flu A/Indonesia/5/05 (1/DIL)	Vaccine Group	S-	136	136	100	97.3	100
		S+	52	41	78.8	65.3	88.9
		Total	188	177	94.1	89.8	97.0
Flu A/Vietnam/1194/04 (1/DIL)	Vaccine Group	S-	108	98	90.7	83.6	95.5
		S+	73	15	20.5	12.0	31.6
		Total	181	113	62.4	54.9	69.5
S- = seronegative subjects (antibody titer < 1:28 for Flu A/Vietnam/1194/04 antibody, Flu A/Indonesia/5/05 antibody) prior to vaccination							
S+ = seropositive subjects (antibody titer ≥ 1:28 for Flu A/Vietnam/1194/04 antibody, Flu A/Indonesia/5/05 antibody) prior to vaccination							
Total = subjects either seropositive or seronegative at pre-vaccination							
Vaccine response defined as antibody titer at Day 42 ≥ 4-fold the pre-vaccination antibody titer							
N = number of subjects with both pre- and post-vaccination results available							
n (%) = number (percentage) of responders							
95% CI = exact 95% confidence interval; LL = lower limit, UL = upper limit							
Day 42 = 42 days post Dose 1							
Secondary Outcome Variables: Vaccine response rate for H5N1 antibodies as assessed by microneutralization assays at Day 42 in subjects greater than 64 years of age (ATP cohort for immunogenicity)							
Antibody	Group	Pre-vaccination status	N	Vaccine response			
				n	%	95% CI	
						LL	UL
Flu A/Indonesia/5/05 (1/DIL)	Vaccine Group	S-	13	13	100	75.3	100
		S+	33	23	69.7	51.3	84.4
		Total	46	36	78.3	63.6	89.1
Flu A/Vietnam/1194/04 (1/DIL)	Vaccine Group	S-	8	7	87.5	47.3	99.7
		S+	36	5	13.9	4.7	29.5
		Total	44	12	27.3	15.0	42.8
S- = seronegative subjects (antibody titer < 1:28 for Flu A/Vietnam/1194/04 antibody, Flu A/Indonesia/5/05 antibody) prior to vaccination							
S+ = seropositive subjects (antibody titer ≥ 1:28 for Flu A/Vietnam/1194/04 antibody, Flu A/Indonesia/5/05 antibody) prior to vaccination							
Total = subjects either seropositive or seronegative at pre-vaccination							
Vaccine response defined as antibody titer at Day 42 ≥ 4-fold the pre-vaccination antibody titer							
N = number of subjects with both pre- and post-vaccination results available							
n (%) = number (percentage) of responders							
95% CI = exact 95% confidence interval; LL = lower limit, UL = upper limit							
Day 42 = 42 days post Dose 1							
Secondary Outcome Variables: GMTs for H5N1 antibodies as assessed by microneutralization assays at Day 42 in subjects between 18 and 64 years of age (ATP cohort for immunogenicity)							
Antibody	Group	Timing	N	GMT			
				value	95% CI		
					LL	UL	
Flu A/Indonesia/5/05	Vaccine Group	PRE	188	22.4	19.9	25.3	
		Day 42	188	1450.6	1266.9	1660.9	
Flu A/Vietnam/1194/04	Vaccine Group	PRE	181	29.9	25.7	34.9	
		Day 42	181	163.1	145.6	182.8	
N = number of subjects with available results							
n (%) = number (percentage) of subjects with titer within the specified range							

95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit PRE = Blood sample taken before vaccination Day 42 = 42 days post Dose 1														
Secondary Outcome Variables: GMTs for H5N1 antibodies as assessed by microneutralization assays at Day 42 in subjects greater than 64 years of age (ATP cohort for immunogenicity)														
Antibody	Group	Timing	N	GMT										
				value	95% CI									
					LL	UL								
Flu A/Indonesia/5/05	Vaccine Group	PRE	46	52.4	39.2	69.8								
		Day 42	46	631.1	444.5	896.1								
Flu A/Vietnam/1194/04	Vaccine Group	PRE	44	94.4	68.4	130.3								
		Day 42	44	213.4	165.5	275.1								
N = number of subjects with available results n (%) = number (percentage) of subjects with titer within the specified range 95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit PRE = Blood sample taken before vaccination Day 42 = 42 days post Dose 1														
Secondary Outcome Variables: SCR for H5N1 antibody at Day 182 in subjects between 18 and 64 years of age (ATP cohort for immunogenicity)														
Group	Pre-vaccination status	N	SCR											
			n	%	95% CI									
					LL	UL								
Vaccine Group	S-	365	224	61.4	56.2	66.4								
	S+	1	1	100	2.5	100								
	Total	366	225	61.5	56.3	66.5								
Placebo Group	S-	37	1	2.7	0.1	14.2								
	S+	0	0	.	.	.								
	Total	37	1	2.7	0.1	14.2								
S- = seronegative subjects (antibody titer < 1:10 for Flu A/Indonesia/5/05 antibody) prior to vaccination S+ = seropositive subjects (antibody titer ≥ 1:10 for Flu A/Indonesia/5/05 antibody) prior to vaccination Total = subjects either seropositive or seronegative at pre-vaccination SCR defined as : For initially seronegative subjects, antibody titer ≥ 1:40 at Day 182 For initially seropositive subjects : antibody titer at Day 182 ≥ 4 fold the pre-vaccination antibody titer N = number of subjects with both pre- and post-vaccination results available n (%) = number (percentage) of responders 95% CI = exact 95% confidence interval; LL = lower limit, UL = upper limit Day 182 = 182 days post Dose 1														
Secondary Outcome Variables: Seropositivity, SPR and GMTs for H5N1 antibodies in subjects between 18 and 64 years of age (ATP cohort for immunogenicity)														
Antibody	Group	Timing	N	≥ 1:10				≥ 1:40				GMT		
				n	%	95% CI		n	%	95% CI		value	95% CI	
						LL	UL			LL	UL		LL	UL
FLU A/IND/05 HA5 AB	Vaccine Group	PRE	1571	5	0.3	0.1	0.7	0	0.0	0.0	0.2	5.0	5.0	5.0
		Day 42	1571	1467	93.4	92.0	94.6	1427	90.8	89.3	92.2	249.0	231.8	267.5
		Day 182	366	258	70.5	65.5	75.1	225	61.5	56.3	66.5	36.2	31.0	42.2
	Placebo Group	PRE	76	0	0.0	0.0	4.7	0	0.0	0.0	4.7	5.0	5.0	5.0
		Day 42	76	1	1.3	0.0	7.1	1	1.3	0.0	7.1	5.1	4.9	5.4
		Day 182	37	2	5.4	0.7	18.2	1	2.7	0.1	14.2	5.5	4.8	6.5
SPR = Flu A/Indonesia/5/05 antibody titer ≥ 1:40 N = number of subjects with available results n (%) = number (percentage) of subjects with titer within the specified range 95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit PRE = Blood sample taken before vaccination														

Day 42 = 42 days post Dose 1 Day 182 = 182 days post Dose 1														
Secondary Outcome Variables: SCR for H5N1 antibody at Day 182 in subjects greater than 64 years of age (ATP cohort for immunogenicity)														
Group	Pre-vaccination status	N	SCR											
			n	%	95% CI									
					LL	UL								
Vaccine Group	S-	90	59	65.6	54.8	75.3								
	S+	1	0	0.0	0.0	97.5								
	Total	91	59	64.8	54.1	74.6								
Placebo Group	S-	19	0	0.0	0.0	17.6								
	S+	0	0	.	.	.								
	Total	19	0	0.0	0.0	17.6								
<p>S- = seronegative subjects (antibody titer < 1:10 for Flu A/Indonesia/5/05 antibody) prior to vaccination S+ = seropositive subjects (antibody titer ≥ 1:10 for Flu A/Indonesia/5/05 antibody) prior to vaccination Total = subjects either seropositive or seronegative at pre-vaccination SCR defined as : For initially seronegative subjects, antibody titer ≥ 1:40 at Day 182 For initially seropositive subjects : antibody titer at Day 182 ≥ 4 fold the pre-vaccination antibody titer N = number of subjects with both pre- and post-vaccination results available n (%) = number (percentage) of responders 95% CI = exact 95% confidence interval; LL = lower limit, UL = upper limit Day 182 = 182 days post Dose 1</p>														
Secondary Outcome Variables: Seropositivity, SPR and GMTs for H5N1 antibodies in subjects greater than 64 years of age (ATP cohort for immunogenicity)														
Antibody	Group	Timing	N	≥ 1:10				≥ 1:40				GMT		
				n	%	95% CI		n	%	95% CI		value	95% CI	
						LL	UL			LL	UL		LL	UL
Flu A/Indonesia/5/05 antibody	Vaccine Group	PRE	396	9	2.3	1.0	4.3	2	0.5	0.1	1.8	5.2	5.1	5.3
		Day 42	396	334	84.3	80.4	87.8	295	74.5	69.9	78.7	81.9	69.7	96.2
		Day 182	91	77	84.6	75.5	91.3	60	65.9	55.3	75.5	44.8	33.3	60.4
	Placebo Group	PRE	40	0	0.0	0.0	8.8	0	0.0	0.0	8.8	5.0	5.0	5.0
		Day 42	40	1	2.5	0.1	13.2	1	2.5	0.1	13.2	5.5	4.5	6.8
		Day 182	19	1	5.3	0.1	26.0	0	0.0	0.0	17.6	5.4	4.6	6.3
<p>SPR = Flu A/Indonesia/5/05 antibody titer ≥ 1:40 N = number of subjects with available results n (%) = number (percentage) of subjects with titer within the specified range 95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit PRE = Blood sample taken before vaccination Day 42 = 42 days post Dose 1 Day 182 = 182 days post Dose 1</p>														
Safety results: Number (%) of subjects with unsolicited AEs occurring within the 21 days (Day 0-20) following each vaccine dose in subjects between 18 and 64 years of age (Total Vaccinated cohort)														
Most frequent adverse events - On-Therapy (occurring within Day 0-20 following vaccination)			Vaccine Group N = 2304		Placebo Group N = 768									
Subjects with any AE(s), n (%)			914 (39.7)		289 (37.6)									
Nasopharyngitis			94 (4.1)		26 (3.4)									
Pharyngolaryngeal pain			85 (3.7)		35 (4.6)									
Nausea			76 (3.3)		20 (2.6)									
Headache			67 (2.9)		25 (3.3)									
Cough			63 (2.7)		27 (3.5)									
Upper respiratory tract infection			61 (2.6)		21 (2.7)									
Nasal congestion			57 (2.5)		19 (2.5)									
Diarrhoea			56 (2.4)		-									
Back pain			36 (1.6)		18 (2.3)									

Sinusitis	39 (1.7)	-
Injection site pruritus	36 (1.6)	-
Rhinorrhoea	-	14 (1.8)
Lymphadenopathy	-	13 (1.7)
- : Adverse event absent or not meeting the selected rule(s): more than 30 subjects per treatment group and ≤ 3 groups: only the 10 most frequent events in each group are to be listed.		
Safety results: Number (%) of subjects with unsolicited AEs occurring within the 21 days (Day 0-20) following each vaccine dose in subjects greater than 64 years of age (Total Vaccinated cohort)		
Most frequent adverse events - On-Therapy (occurring within Day 0-20 following vaccination)	Vaccine Group N = 1118	Placebo Group N = 371
Subjects with any AE(s), n (%)	399 (35.7)	113 (30.5)
Pharyngolaryngeal pain	33 (3.0)	12 (3.2)
Nasopharyngitis	34 (3.0)	10 (2.7)
Diarrhoea	33 (3.0)	10 (2.7)
Cough	26 (2.3)	6 (1.6)
Headache	24 (2.1)	7 (1.9)
Upper respiratory tract infection	21 (1.9)	8 (2.2)
Pain in extremity	19 (1.7)	4 (1.1)
Back pain	20 (1.8)	-
Injection site pruritus	20 (1.8)	-
Nausea	19 (1.7)	-
Influenza like illness	-	8 (2.2)
Bronchitis	-	6 (1.6)
Musculoskeletal pain	-	5 (1.3)
Sinusitis	-	4 (1.1)
- : Adverse event absent or not meeting the selected rule(s): more than 30 subjects per treatment group and ≤ 3 groups: only the 10 most frequent events in each group are to be listed.		
Safety results: Number (%) of subjects with unsolicited AEs occurring during Days 0-84 in subjects between 18 and 64 years of age (Total Vaccinated cohort)		
Most frequent adverse events - On-Therapy (occurring within Day 0-84)	Vaccine Group N = 2304	Placebo Group N = 768
Subjects with any AE(s), n (%)	1017 (44.1)	321 (41.8)
Nasopharyngitis	116 (5.0)	29 (3.8)
Oropharyngeal pain	91 (3.9)	39 (5.1)
Headache	73 (3.2)	31 (4.0)
Nausea	78 (3.4)	20 (2.6)
Upper respiratory tract infection	73 (3.2)	25 (3.3)
Cough	66 (2.9)	28 (3.6)
Nasal congestion	59 (2.6)	20 (2.6)
Diarrhoea	57 (2.5)	14 (1.8)
Back pain	43 (1.9)	19 (2.5)
Sinusitis	56 (2.4)	-
Lymphadenopathy	-	14 (1.8)
Rhinorrhoea	-	14 (1.8)
- : Adverse event absent or not meeting the selected rule(s): more than 30 subjects per treatment group and ≤ 3 groups: only the 10 most frequent events in each group are to be listed.		
Safety results: Number (%) of subjects with unsolicited AEs occurring during Days 0-84 in subjects greater than 64 years of age (Total Vaccinated cohort)		
Most frequent adverse events - On-Therapy (occurring within Day 0-84)	Vaccine Group N = 1118	Placebo Group N = 371
Subjects with any AE(s), n (%)	467 (41.8)	130 (35.0)
Nasopharyngitis	40 (3.6)	11 (3.0)
Oropharyngeal pain	34 (3.0)	12 (3.2)
Diarrhoea	34 (3.0)	11 (3.0)

Upper respiratory tract infection	27 (2.4)	13 (3.5)
Headache	28 (2.5)	8 (2.2)
Cough	29 (2.6)	6 (1.6)
Injection site pruritus	23 (2.1)	-
Back pain	21 (1.9)	-
Nausea	20 (1.8)	-
Pain in extremity	19 (1.7)	-
Influenza like illness	-	8 (2.2)
Bronchitis	-	7 (1.9)
Musculoskeletal pain	-	5 (1.3)
Sinusitis	-	5 (1.3)
- : Adverse event absent or not meeting the selected rule(s): more than 30 subjects per treatment group and ≤ 3 groups: only the 10 most frequent events in each group are to be listed.		
Safety results: Number (%) of subjects with SAEs occurring within Day 0-182 in subjects between 18 and 64 years of age. (Total Vaccinated cohort)		
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]		
All SAEs (occurring within Day 0-182)	Vaccine Group N = 2304	Placebo Group N = 768
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	24 (1.0) [0]	7 (0.9) [0]
Chest pain	2 (0.1) [0]	0 (0.0) [0]
Abdominal hernia	1 (0.0) [0]	0 (0.0) [0]
Adjustment disorder with mixed anxiety and depressed mood	1 (0.0) [0]	0 (0.0) [0]
Affective disorder	1 (0.0) [0]	0 (0.0) [0]
Anaphylactic reaction	1 (0.0) [0]	0 (0.0) [0]
Atrial fibrillation	1 (0.0) [0]	0 (0.0) [0]
Atrial septal defect	0 (0.0) [0]	1 (0.1) [0]
Breast cancer recurrent	1 (0.0) [0]	0 (0.0) [0]
Caecitis	1 (0.0) [0]	0 (0.0) [0]
Cardiomegaly	0 (0.0) [0]	1 (0.1) [0]
Carotid artery dissection	0 (0.0) [0]	1 (0.1) [0]
Cellulitis	1 (0.0) [0]	0 (0.0) [0]
Cerebrovascular accident	0 (0.0) [0]	1 (0.1) [0]
Colon cancer	1 (0.0) [0]	0 (0.0) [0]
Convulsion	1 (0.0) [0]	0 (0.0) [0]
Coronary artery disease	0 (0.0) [0]	1 (0.1) [0]
Diabetes mellitus	1 (0.0) [0]	0 (0.0) [0]
Diarrhoea infectious	0 (0.0) [0]	1 (0.1) [0]
Dyspepsia	1 (0.0) [0]	0 (0.0) [0]
Hypertrophic cardiomyopathy	1 (0.0) [0]	0 (0.0) [0]
Intervertebral disc protrusion	1 (0.0) [0]	0 (0.0) [0]
Ischaemic stroke	1 (0.0) [0]	0 (0.0) [0]
Liver disorder	1 (0.0) [0]	0 (0.0) [0]
Mania	1 (0.0) [0]	0 (0.0) [0]
Mental disorder	1 (0.0) [0]	0 (0.0) [0]
Myocardial infarction	1 (0.0) [0]	0 (0.0) [0]
Neonatal respiratory failure	0 (0.0) [0]	1 (0.1) [0]
Osteoarthritis	0 (0.0) [0]	1 (0.1) [0]
Pneumonia	1 (0.0) [0]	0 (0.0) [0]
Pneumonia bacterial	0 (0.0) [0]	1 (0.1) [0]
Pneumonia pneumococcal	0 (0.0) [0]	1 (0.1) [0]
Pulmonary embolism	1 (0.0) [0]	0 (0.0) [0]
Small intestinal obstruction	1 (0.0) [0]	0 (0.0) [0]
Spinal column stenosis	0 (0.0) [0]	1 (0.1) [0]

Syncope	1 (0.0) [0]	0 (0.0) [0]
Transplant rejection	1 (0.0) [0]	0 (0.0) [0]
Fatal SAEs	Vaccine Group N = 2304	Placebo Group N = 768
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	2 (0.1) [0]	1 (0.1) [0]
Cardiomegaly	0 (0.0) [0]	1 (0.1) [0]
Diabetes mellitus	1 (0.0) [0]	0 (0.0) [0]
Liver disorder	1 (0.0) [0]	0 (0.0) [0]
Myocardial infarction	1 (0.0) [0]	0 (0.0) [0]
Safety results: Number (%) of subjects with SAEs occurring within Day 0-182 in subjects greater than 64 years of age (Total Vaccinated cohort)		
All SAEs (occurring within Day 0-182)	Vaccine Group N = 1118	Placebo Group N = 371
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	43 (3.8) [0]	14 (3.8) [0]
Pneumonia	4 (0.4) [0]	1 (0.3) [0]
Atrial fibrillation	2 (0.2) [0]	1 (0.3) [0]
Myocardial infarction	3 (0.3) [0]	0 (0.0) [0]
Cerebrovascular accident	2 (0.2) [0]	0 (0.0) [0]
Deep vein thrombosis	2 (0.2) [0]	0 (0.0) [0]
Diastolic dysfunction	1 (0.1) [0]	1 (0.3) [0]
Intestinal obstruction	2 (0.2) [0]	0 (0.0) [0]
Pulmonary embolism	2 (0.2) [0]	0 (0.0) [0]
Thyroid cancer	2 (0.2) [0]	0 (0.0) [0]
Transient ischaemic attack	1 (0.1) [0]	1 (0.3) [0]
Acute coronary syndrome	0 (0.0) [0]	1 (0.3) [0]
Aneurysm	1 (0.1) [0]	0 (0.0) [0]
Angina unstable	0 (0.0) [0]	1 (0.3) [0]
Aortic aneurysm	1 (0.1) [0]	0 (0.0) [0]
Appendicitis	1 (0.1) [0]	0 (0.0) [0]
Arthralgia	1 (0.1) [0]	0 (0.0) [0]
Arthritis bacterial	1 (0.1) [0]	0 (0.0) [0]
Biopsy liver normal	1 (0.1) [0]	0 (0.0) [0]
Brain neoplasm malignant	0 (0.0) [0]	1 (0.3) [0]
Breast cancer	1 (0.1) [0]	0 (0.0) [0]
Bronchitis	1 (0.1) [0]	0 (0.0) [0]
Cardiac failure congestive	0 (0.0) [0]	1 (0.3) [0]
Carotid artery stenosis	1 (0.1) [0]	0 (0.0) [0]
Cellulitis	1 (0.1) [0]	0 (0.0) [0]
Chest pain	1 (0.1) [0]	0 (0.0) [0]
Cholangitis suppurative	1 (0.1) [0]	0 (0.0) [0]
Colitis	1 (0.1) [0]	0 (0.0) [0]
Colitis ischaemic	0 (0.0) [0]	1 (0.3) [0]
Coronary artery stenosis	0 (0.0) [0]	1 (0.3) [0]
Diverticulitis	1 (0.1) [0]	0 (0.0) [0]
Enteritis	0 (0.0) [0]	1 (0.3) [0]
Gastritis	1 (0.1) [0]	0 (0.0) [0]
Gastrointestinal haemorrhage	0 (0.0) [0]	1 (0.3) [0]
Gout	1 (0.1) [0]	0 (0.0) [0]
Hamartoma	1 (0.1) [0]	0 (0.0) [0]
Herpes zoster	1 (0.1) [0]	0 (0.0) [0]
Hip fracture	0 (0.0) [0]	1 (0.3) [0]
Hypotension	1 (0.1) [0]	0 (0.0) [0]

Ileus	1 (0.1) [0]	0 (0.0) [0]
Large intestine perforation	1 (0.1) [0]	0 (0.0) [0]
Left atrial dilatation	1 (0.1) [0]	0 (0.0) [0]
Lower gastrointestinal haemorrhage	1 (0.1) [0]	0 (0.0) [0]
Lung neoplasm malignant	1 (0.1) [0]	0 (0.0) [0]
Lymphoma	1 (0.1) [0]	0 (0.0) [0]
Melaena	1 (0.1) [0]	0 (0.0) [0]
Mental status changes	0 (0.0) [0]	1 (0.3) [0]
Metastases to liver	1 (0.1) [0]	0 (0.0) [0]
Musculoskeletal pain	0 (0.0) [0]	1 (0.3) [0]
Nasal septum deviation	0 (0.0) [0]	1 (0.3) [0]
Neoplasm malignant	1 (0.1) [0]	0 (0.0) [0]
Nephrolithiasis	1 (0.1) [0]	0 (0.0) [0]
Osteoarthritis	1 (0.1) [0]	0 (0.0) [0]
Ovarian cancer metastatic	1 (0.1) [0]	0 (0.0) [0]
Renal cancer	0 (0.0) [0]	1 (0.3) [0]
Renal tubular acidosis	1 (0.1) [0]	0 (0.0) [0]
Renal vessel disorder	1 (0.1) [0]	0 (0.0) [0]
Rib fracture	1 (0.1) [0]	0 (0.0) [0]
Rotator cuff syndrome	1 (0.1) [0]	0 (0.0) [0]
Sepsis	1 (0.1) [0]	0 (0.0) [0]
Sick sinus syndrome	1 (0.1) [0]	0 (0.0) [0]
Small intestinal obstruction	1 (0.1) [0]	0 (0.0) [0]
Spinal cord compression	1 (0.1) [0]	0 (0.0) [0]
Spondylolisthesis	1 (0.1) [0]	0 (0.0) [0]
Subcutaneous abscess	1 (0.1) [0]	0 (0.0) [0]
Urinary retention postoperative	1 (0.1) [0]	0 (0.0) [0]
Viral infection	1 (0.1) [0]	0 (0.0) [0]
Fatal SAEs	Vaccine Group N = 1118	Placebo Group N = 371
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	2 (0.2) [0]	1 (0.3) [0]
Brain neoplasm malignant	0 (0.0) [0]	1 (0.3) [0]
Metastases to liver	1 (0.1) [0]	0 (0.0) [0]
Neoplasm malignant	1 (0.1) [0]	0 (0.0) [0]
Ovarian cancer metastatic	1 (0.1) [0]	0 (0.0) [0]
Safety results: Number (%) of subjects with SAEs occurring within Day 0-379* in subjects between 18 and 64 years of age (Total Vaccinated cohort)		
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]		
All SAEs (occurring within Day 0-379)	Vaccine Group N = 2304	Placebo Group N = 768
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	46 (2.0) [0]	15 (2.0) [0]
Pneumonia	1 (0.0) [0]	0 (0.0) [0]
Myocardial infarction	1 (0.0) [0]	0 (0.0) [0]
Chest pain	3 (0.1) [0]	0 (0.0) [0]
Osteoarthritis	0 (0.0) [0]	1 (0.1) [0]
Atrial fibrillation	1 (0.0) [0]	0 (0.0) [0]
Cerebrovascular accident	0 (0.0) [0]	1 (0.1) [0]
Cellulitis	1 (0.0) [0]	1 (0.1) [0]
Convulsion	2 (0.1) [0]	0 (0.0) [0]
Coronary artery disease	0 (0.0) [0]	1 (0.1) [0]
Pulmonary embolism	1 (0.0) [0]	0 (0.0) [0]
Thyroid cancer	1 (0.0) [0]	0 (0.0) [0]
Abdominal hernia	2 (0.1) [0]	0 (0.0) [0]

Abortion spontaneous	2 (0.1) [0]	0 (0.0) [0]
Acute coronary syndrome	0 (0.0) [0]	0 (0.0) [0]
Angina unstable	0 (0.0) [0]	0 (0.0) [0]
Appendicitis	0 (0.0) [0]	0 (0.0) [0]
Back pain	0 (0.0) [0]	0 (0.0) [0]
Breast cancer	1 (0.0) [0]	0 (0.0) [0]
Calculus bladder	1 (0.0) [0]	0 (0.0) [0]
Coronary artery stenosis	0 (0.0) [0]	0 (0.0) [0]
Deep vein thrombosis	0 (0.0) [0]	0 (0.0) [0]
Diabetes mellitus	1 (0.0) [0]	0 (0.0) [0]
Diastolic dysfunction	0 (0.0) [0]	0 (0.0) [0]
Diverticulitis	0 (0.0) [0]	0 (0.0) [0]
Intervertebral disc protrusion	2 (0.1) [0]	0 (0.0) [0]
Intestinal obstruction	0 (0.0) [0]	0 (0.0) [0]
Large intestine perforation	0 (0.0) [0]	0 (0.0) [0]
Lung neoplasm malignant	0 (0.0) [0]	0 (0.0) [0]
Nephrolithiasis	0 (0.0) [0]	0 (0.0) [0]
Sepsis	1 (0.0) [0]	0 (0.0) [0]
Small intestinal obstruction	1 (0.0) [0]	0 (0.0) [0]
Staphylococcal infection	1 (0.0) [0]	0 (0.0) [0]
Transient ischaemic attack	0 (0.0) [0]	0 (0.0) [0]
Abdominal pain	0 (0.0) [0]	0 (0.0) [0]
Acute myocardial infarction	0 (0.0) [0]	0 (0.0) [0]
Affective disorder	1 (0.0) [0]	0 (0.0) [0]
Anaphylactic reaction	1 (0.0) [0]	0 (0.0) [0]
Aneurysm	0 (0.0) [0]	0 (0.0) [0]
Ankle fracture	1 (0.0) [0]	0 (0.0) [0]
Aortic aneurysm	0 (0.0) [0]	0 (0.0) [0]
Arthralgia	0 (0.0) [0]	0 (0.0) [0]
Arthritis bacterial	0 (0.0) [0]	0 (0.0) [0]
Atrial septal defect	0 (0.0) [0]	1 (0.1) [0]
Biliary dyskinesia	0 (0.0) [0]	1 (0.1) [0]
Biopsy liver normal	0 (0.0) [0]	0 (0.0) [0]
Brain neoplasm malignant	0 (0.0) [0]	0 (0.0) [0]
Breast cancer recurrent	1 (0.0) [0]	0 (0.0) [0]
Bronchitis	0 (0.0) [0]	0 (0.0) [0]
Caecitis	1 (0.0) [0]	0 (0.0) [0]
Cardiac disorder	0 (0.0) [0]	0 (0.0) [0]
Cardiac failure congestive	0 (0.0) [0]	0 (0.0) [0]
Cardiomegaly	0 (0.0) [0]	1 (0.1) [0]
Carotid artery dissection	0 (0.0) [0]	1 (0.1) [0]
Carotid artery stenosis	0 (0.0) [0]	0 (0.0) [0]
Cholangitis suppurative	0 (0.0) [0]	0 (0.0) [0]
Cholecystitis	1 (0.0) [0]	0 (0.0) [0]
Cholelithiasis	1 (0.0) [0]	0 (0.0) [0]
Chronic obstructive pulmonary disease	0 (0.0) [0]	0 (0.0) [0]
Colitis	0 (0.0) [0]	0 (0.0) [0]
Colitis ischaemic	0 (0.0) [0]	0 (0.0) [0]
Colon cancer	1 (0.0) [0]	0 (0.0) [0]
Contusion	1 (0.0) [0]	0 (0.0) [0]
Coronary artery occlusion	0 (0.0) [0]	0 (0.0) [0]
Depression	1 (0.0) [0]	0 (0.0) [0]
Diabetic complication	0 (0.0) [0]	1 (0.1) [0]
Diabetic ketoacidosis	1 (0.0) [0]	0 (0.0) [0]
Diarrhoea	1 (0.0) [0]	0 (0.0) [0]
Diarrhoea infectious	0 (0.0) [0]	1 (0.1) [0]

Dyspepsia	1 (0.0) [0]	0 (0.0) [0]
Enteritis	0 (0.0) [0]	0 (0.0) [0]
Febrile neutropenia	0 (0.0) [0]	0 (0.0) [0]
Fibula fracture	1 (0.0) [0]	0 (0.0) [0]
Forearm fracture	0 (0.0) [0]	0 (0.0) [0]
Gallbladder disorder	0 (0.0) [0]	1 (0.1) [0]
Gastritis	0 (0.0) [0]	0 (0.0) [0]
Gastrointestinal haemorrhage	0 (0.0) [0]	0 (0.0) [0]
Gastrooesophageal reflux disease	0 (0.0) [0]	0 (0.0) [0]
Gout	0 (0.0) [0]	0 (0.0) [0]
Hiv test positive	0 (0.0) [0]	1 (0.1) [0]
Hamartoma	0 (0.0) [0]	0 (0.0) [0]
Hepatitis	0 (0.0) [0]	0 (0.0) [0]
Herpes zoster	0 (0.0) [0]	0 (0.0) [0]
Hiatus hernia	0 (0.0) [0]	0 (0.0) [0]
Hip fracture	0 (0.0) [0]	0 (0.0) [0]
Humerus fracture	0 (0.0) [0]	0 (0.0) [0]
Hypersensitivity	0 (0.0) [0]	0 (0.0) [0]
Hyperthyroidism	1 (0.0) [0]	0 (0.0) [0]
Hypertrophic cardiomyopathy	1 (0.0) [0]	0 (0.0) [0]
Hypotension	0 (0.0) [0]	0 (0.0) [0]
Ileus	0 (0.0) [0]	0 (0.0) [0]
Ischaemic stroke	1 (0.0) [0]	0 (0.0) [0]
Left atrial dilatation	0 (0.0) [0]	0 (0.0) [0]
Liver disorder	1 (0.0) [0]	0 (0.0) [0]
Lower gastrointestinal haemorrhage	0 (0.0) [0]	0 (0.0) [0]
Lymph node cancer metastatic	1 (0.0) [0]	0 (0.0) [0]
Lymphoma	0 (0.0) [0]	0 (0.0) [0]
Major depression	1 (0.0) [0]	0 (0.0) [0]
Mania	1 (0.0) [0]	0 (0.0) [0]
Melaena	0 (0.0) [0]	0 (0.0) [0]
Meniscus lesion	0 (0.0) [0]	0 (0.0) [0]
Mental disorder	1 (0.0) [0]	0 (0.0) [0]
Mental status changes	0 (0.0) [0]	0 (0.0) [0]
Metastases to liver	0 (0.0) [0]	0 (0.0) [0]
Migraine	1 (0.0) [0]	0 (0.0) [0]
Mountain sickness acute	0 (0.0) [0]	0 (0.0) [0]
Muscle strain	1 (0.0) [0]	0 (0.0) [0]
Musculoskeletal pain	0 (0.0) [0]	0 (0.0) [0]
Nasal septum deviation	0 (0.0) [0]	0 (0.0) [0]
Neonatal respiratory failure	0 (0.0) [0]	1 (0.1) [0]
Neoplasm malignant	0 (0.0) [0]	0 (0.0) [0]
Non-cardiac chest pain	1 (0.0) [0]	0 (0.0) [0]
Ovarian cancer metastatic	0 (0.0) [0]	0 (0.0) [0]
Pancreatitis	0 (0.0) [0]	0 (0.0) [0]
Peripheral vascular disorder	1 (0.0) [0]	0 (0.0) [0]
Pneumonia bacterial	0 (0.0) [0]	1 (0.1) [0]
Pneumonia pneumococcal	0 (0.0) [0]	1 (0.1) [0]
Pyelonephritis	1 (0.0) [0]	0 (0.0) [0]
Radiculitis	0 (0.0) [0]	0 (0.0) [0]
Rectal cancer stage 0	0 (0.0) [0]	0 (0.0) [0]
Renal cancer	0 (0.0) [0]	0 (0.0) [0]
Renal failure	0 (0.0) [0]	0 (0.0) [0]
Renal failure acute	0 (0.0) [0]	1 (0.1) [0]
Renal tubular acidosis	0 (0.0) [0]	0 (0.0) [0]
Renal vessel disorder	0 (0.0) [0]	0 (0.0) [0]

Rib fracture	0 (0.0) [0]	0 (0.0) [0]
Rotator cuff syndrome	0 (0.0) [0]	0 (0.0) [0]
Seminoma	0 (0.0) [0]	1 (0.1) [0]
Sick sinus syndrome	0 (0.0) [0]	0 (0.0) [0]
Spinal column stenosis	0 (0.0) [0]	1 (0.1) [0]
Spinal compression fracture	0 (0.0) [0]	0 (0.0) [0]
Spinal cord compression	0 (0.0) [0]	0 (0.0) [0]
Spondylolisthesis	0 (0.0) [0]	0 (0.0) [0]
Subcutaneous abscess	0 (0.0) [0]	0 (0.0) [0]
Syncope	1 (0.0) [0]	0 (0.0) [0]
Synovial cyst	0 (0.0) [0]	0 (0.0) [0]
Tibia fracture	0 (0.0) [0]	0 (0.0) [0]
Tongue carcinoma stage i	1 (0.0) [0]	0 (0.0) [0]
Tongue neoplasm malignant stage unspecified	0 (0.0) [0]	0 (0.0) [0]
Toxic nodular goitre	0 (0.0) [0]	1 (0.1) [0]
Tracheobronchitis	0 (0.0) [0]	1 (0.1) [0]
Transplant rejection	1 (0.0) [0]	0 (0.0) [0]
Ulna fracture	0 (0.0) [0]	0 (0.0) [0]
Urinary retention postoperative	0 (0.0) [0]	0 (0.0) [0]
Urinary tract infection	0 (0.0) [0]	0 (0.0) [0]
Viral infection	0 (0.0) [0]	0 (0.0) [0]
Fatal SAEs	Vaccine Group N = 2304	Placebo Group N = 768
subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	2 (0.1) [0]	1 (0.1) [0]
Brain neoplasm malignant	0 (0.0) [0]	0 (0.0) [0]
Cardiac disorder	0 (0.0) [0]	0 (0.0) [0]
Cardiomegaly	0 (0.0) [0]	1 (0.1) [0]
Diabetes mellitus	1 (0.0) [0]	0 (0.0) [0]
Liver disorder	1 (0.0) [0]	0 (0.0) [0]
Metastases to liver	0 (0.0) [0]	0 (0.0) [0]
Myocardial infarction	1 (0.0) [0]	0 (0.0) [0]
Neoplasm malignant	0 (0.0) [0]	0 (0.0) [0]
Ovarian cancer metastatic	0 (0.0) [0]	0 (0.0) [0]
Pneumonia	0 (0.0) [0]	0 (0.0) [0]
Tongue neoplasm malignant stage unspecified	0 (0.0) [0]	0 (0.0) [0]
* SAEs were collected through Day 379 (the limit of the contact window for Day 364 was through Day 379).		
Safety results: Number (%) of subjects with SAEs occurring within Day 0-379* in subjects greater than 64 years of age (Total Vaccinated cohort)		
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]		
All SAEs (occurring within Day 0-379)	Vaccine Group N = 1118	Placebo Group N = 371
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	65 (5.8) [0]	30 (8.1) [0]
Pneumonia	4 (0.4) [0]	2 (0.5) [0]
Myocardial infarction	3 (0.3) [0]	2 (0.5) [0]
Chest pain	2 (0.2) [0]	0 (0.0) [0]
Osteoarthritis	3 (0.3) [0]	1 (0.3) [0]
Atrial fibrillation	2 (0.2) [0]	1 (0.3) [0]
Cerebrovascular accident	3 (0.3) [0]	0 (0.0) [0]
Cellulitis	1 (0.1) [0]	0 (0.0) [0]
Convulsion	1 (0.1) [0]	0 (0.0) [0]
Coronary artery disease	1 (0.1) [0]	1 (0.3) [0]
Pulmonary embolism	2 (0.2) [0]	0 (0.0) [0]
Thyroid cancer	2 (0.2) [0]	0 (0.0) [0]
Abdominal hernia	0 (0.0) [0]	0 (0.0) [0]

Abortion spontaneous	0 (0.0) [0]	0 (0.0) [0]
Acute coronary syndrome	0 (0.0) [0]	2 (0.5) [0]
Angina unstable	1 (0.1) [0]	1 (0.3) [0]
Appendicitis	2 (0.2) [0]	0 (0.0) [0]
Back pain	2 (0.2) [0]	0 (0.0) [0]
Breast cancer	1 (0.1) [0]	0 (0.0) [0]
Calculus bladder	1 (0.1) [0]	0 (0.0) [0]
Coronary artery stenosis	0 (0.0) [0]	2 (0.5) [0]
Deep vein thrombosis	2 (0.2) [0]	0 (0.0) [0]
Diabetes mellitus	1 (0.1) [0]	0 (0.0) [0]
Diastolic dysfunction	1 (0.1) [0]	1 (0.3) [0]
Diverticulitis	2 (0.2) [0]	0 (0.0) [0]
Intervertebral disc protrusion	0 (0.0) [0]	0 (0.0) [0]
Intestinal obstruction	2 (0.2) [0]	0 (0.0) [0]
Large intestine perforation	1 (0.1) [0]	1 (0.3) [0]
Lung neoplasm malignant	1 (0.1) [0]	1 (0.3) [0]
Nephrolithiasis	2 (0.2) [0]	0 (0.0) [0]
Sepsis	1 (0.1) [0]	0 (0.0) [0]
Small intestinal obstruction	1 (0.1) [0]	0 (0.0) [0]
Staphylococcal infection	0 (0.0) [0]	1 (0.3) [0]
Transient ischaemic attack	1 (0.1) [0]	1 (0.3) [0]
Abdominal pain	1 (0.1) [0]	0 (0.0) [0]
Acute myocardial infarction	1 (0.1) [0]	0 (0.0) [0]
Affective disorder	0 (0.0) [0]	0 (0.0) [0]
Anaphylactic reaction	0 (0.0) [0]	0 (0.0) [0]
Aneurysm	1 (0.1) [0]	0 (0.0) [0]
Ankle fracture	0 (0.0) [0]	0 (0.0) [0]
Aortic aneurysm	1 (0.1) [0]	0 (0.0) [0]
Arthralgia	1 (0.1) [0]	0 (0.0) [0]
Arthritis bacterial	1 (0.1) [0]	0 (0.0) [0]
Atrial septal defect	0 (0.0) [0]	0 (0.0) [0]
Biliary dyskinesia	0 (0.0) [0]	0 (0.0) [0]
Biopsy liver normal	1 (0.1) [0]	0 (0.0) [0]
Brain neoplasm malignant	0 (0.0) [0]	1 (0.3) [0]
Breast cancer recurrent	0 (0.0) [0]	0 (0.0) [0]
Bronchitis	1 (0.1) [0]	0 (0.0) [0]
Caecitis	0 (0.0) [0]	0 (0.0) [0]
Cardiac disorder	0 (0.0) [0]	1 (0.3) [0]
Cardiac failure congestive	0 (0.0) [0]	1 (0.3) [0]
Cardiomegaly	0 (0.0) [0]	0 (0.0) [0]
Carotid artery dissection	0 (0.0) [0]	0 (0.0) [0]
Carotid artery stenosis	1 (0.1) [0]	0 (0.0) [0]
Cholangitis suppurative	1 (0.1) [0]	0 (0.0) [0]
Cholecystitis	0 (0.0) [0]	0 (0.0) [0]
Cholelithiasis	0 (0.0) [0]	0 (0.0) [0]
Chronic obstructive pulmonary disease	1 (0.1) [0]	0 (0.0) [0]
Colitis	1 (0.1) [0]	0 (0.0) [0]
Colitis ischaemic	0 (0.0) [0]	1 (0.3) [0]
Colon cancer	0 (0.0) [0]	0 (0.0) [0]
Contusion	0 (0.0) [0]	0 (0.0) [0]
Coronary artery occlusion	0 (0.0) [0]	1 (0.3) [0]
Depression	0 (0.0) [0]	0 (0.0) [0]
Diabetic complication	0 (0.0) [0]	0 (0.0) [0]
Diabetic ketoacidosis	0 (0.0) [0]	0 (0.0) [0]
Diarrhoea	0 (0.0) [0]	0 (0.0) [0]
Diarrhoea infectious	0 (0.0) [0]	0 (0.0) [0]

Dyspepsia	0 (0.0) [0]	0 (0.0) [0]
Enteritis	0 (0.0) [0]	1 (0.3) [0]
Febrile neutropenia	0 (0.0) [0]	1 (0.3) [0]
Fibula fracture	0 (0.0) [0]	0 (0.0) [0]
Forearm fracture	0 (0.0) [0]	1 (0.3) [0]
Gallbladder disorder	0 (0.0) [0]	0 (0.0) [0]
Gastritis	1 (0.1) [0]	0 (0.0) [0]
Gastrointestinal haemorrhage	0 (0.0) [0]	1 (0.3) [0]
Gastrooesophageal reflux disease	1 (0.1) [0]	0 (0.0) [0]
Gout	1 (0.1) [0]	0 (0.0) [0]
Hiv test positive	0 (0.0) [0]	0 (0.0) [0]
Hamartoma	1 (0.1) [0]	0 (0.0) [0]
Hepatitis	1 (0.1) [0]	0 (0.0) [0]
Herpes zoster	1 (0.1) [0]	0 (0.0) [0]
Hiatus hernia	0 (0.0) [0]	1 (0.3) [0]
Hip fracture	0 (0.0) [0]	1 (0.3) [0]
Humerus fracture	0 (0.0) [0]	1 (0.3) [0]
Hypersensitivity	0 (0.0) [0]	1 (0.3) [0]
Hyperthyroidism	0 (0.0) [0]	0 (0.0) [0]
Hypertrophic cardiomyopathy	0 (0.0) [0]	0 (0.0) [0]
Hypotension	1 (0.1) [0]	0 (0.0) [0]
Ileus	1 (0.1) [0]	0 (0.0) [0]
Ischaemic stroke	0 (0.0) [0]	0 (0.0) [0]
Left atrial dilatation	1 (0.1) [0]	0 (0.0) [0]
Liver disorder	0 (0.0) [0]	0 (0.0) [0]
Lower gastrointestinal haemorrhage	1 (0.1) [0]	0 (0.0) [0]
Lymph node cancer metastatic	0 (0.0) [0]	0 (0.0) [0]
Lymphoma	1 (0.1) [0]	0 (0.0) [0]
Major depression	0 (0.0) [0]	0 (0.0) [0]
Mania	0 (0.0) [0]	0 (0.0) [0]
Melaena	1 (0.1) [0]	0 (0.0) [0]
Meniscus lesion	1 (0.1) [0]	0 (0.0) [0]
Mental disorder	0 (0.0) [0]	0 (0.0) [0]
Mental status changes	0 (0.0) [0]	1 (0.3) [0]
Metastases to liver	1 (0.1) [0]	0 (0.0) [0]
Migraine	0 (0.0) [0]	0 (0.0) [0]
Mountain sickness acute	1 (0.1) [0]	0 (0.0) [0]
Muscle strain	0 (0.0) [0]	0 (0.0) [0]
Musculoskeletal pain	0 (0.0) [0]	1 (0.3) [0]
Nasal septum deviation	0 (0.0) [0]	1 (0.3) [0]
Neonatal respiratory failure	0 (0.0) [0]	0 (0.0) [0]
Neoplasm malignant	1 (0.1) [0]	0 (0.0) [0]
Non-cardiac chest pain	0 (0.0) [0]	0 (0.0) [0]
Ovarian cancer metastatic	1 (0.1) [0]	0 (0.0) [0]
Pancreatitis	1 (0.1) [0]	0 (0.0) [0]
Peripheral vascular disorder	0 (0.0) [0]	0 (0.0) [0]
Pneumonia bacterial	0 (0.0) [0]	0 (0.0) [0]
Pneumonia pneumococcal	0 (0.0) [0]	0 (0.0) [0]
Pyelonephritis	0 (0.0) [0]	0 (0.0) [0]
Radiculitis	1 (0.1) [0]	0 (0.0) [0]
Rectal cancer stage 0	1 (0.1) [0]	0 (0.0) [0]
Renal cancer	0 (0.0) [0]	1 (0.3) [0]
Renal failure	0 (0.0) [0]	1 (0.3) [0]
Renal failure acute	0 (0.0) [0]	0 (0.0) [0]
Renal tubular acidosis	1 (0.1) [0]	0 (0.0) [0]
Renal vessel disorder	1 (0.1) [0]	0 (0.0) [0]

Rib fracture	1 (0.1) [0]	0 (0.0) [0]
Rotator cuff syndrome	1 (0.1) [0]	0 (0.0) [0]
Seminoma	0 (0.0) [0]	0 (0.0) [0]
Sick sinus syndrome	1 (0.1) [0]	0 (0.0) [0]
Spinal column stenosis	0 (0.0) [0]	0 (0.0) [0]
Spinal compression fracture	0 (0.0) [0]	1 (0.3) [0]
Spinal cord compression	1 (0.1) [0]	0 (0.0) [0]
Spondylolisthesis	1 (0.1) [0]	0 (0.0) [0]
Subcutaneous abscess	1 (0.1) [0]	0 (0.0) [0]
Syncope	0 (0.0) [0]	0 (0.0) [0]
Synovial cyst	1 (0.1) [0]	0 (0.0) [0]
Tibia fracture	1 (0.1) [0]	0 (0.0) [0]
Tongue carcinoma stage i	0 (0.0) [0]	0 (0.0) [0]
Tongue neoplasm malignant stage unspecified	0 (0.0) [0]	1 (0.3) [0]
Toxic nodular goitre	0 (0.0) [0]	0 (0.0) [0]
Tracheobronchitis	0 (0.0) [0]	0 (0.0) [0]
Transplant rejection	0 (0.0) [0]	0 (0.0) [0]
Ulna fracture	0 (0.0) [0]	1 (0.3) [0]
Urinary retention postoperative	1 (0.1) [0]	0 (0.0) [0]
Urinary tract infection	0 (0.0) [0]	1 (0.3) [0]
Viral infection	1 (0.1) [0]	0 (0.0) [0]
Fatal SAEs	Vaccine Group N = 1118	Placebo Group N = 371
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	2 (0.2) [0]	4 (1.1) [0]
Brain neoplasm malignant	0 (0.0) [0]	1 (0.3) [0]
Cardiac disorder	0 (0.0) [0]	1 (0.3) [0]
Cardiomegaly	0 (0.0) [0]	0 (0.0) [0]
Diabetes mellitus	0 (0.0) [0]	0 (0.0) [0]
Liver disorder	0 (0.0) [0]	0 (0.0) [0]
Metastases to liver	1 (0.1) [0]	0 (0.0) [0]
Myocardial infarction	0 (0.0) [0]	0 (0.0) [0]
Neoplasm malignant	1 (0.1) [0]	0 (0.0) [0]
Ovarian cancer metastatic	1 (0.1) [0]	0 (0.0) [0]
Pneumonia	0 (0.0) [0]	1 (0.3) [0]
Tongue neoplasm malignant stage unspecified	0 (0.0) [0]	1 (0.3) [0]
* SAEs were collected through Day 379 (the limit of the contact window for Day 364 was through Day 379).		

Conclusion: In the Vaccine Group, the SCRs were 90.8% for the 18 to 64 years age stratum and 74% for the > 64 years age stratum. In the Placebo Group the SCRs were at least 1.3% for the 18 to 64 years age stratum and 2.5% for the > 64 years age stratum. At Day 42, subjects in the 18 to 64 years age stratum of the Vaccine Group had a SPR of 90.8% and subjects in the > 64 years age stratum had a SPR of 74.5%. These values were respectively 1.3% and 2.5% in the Placebo Group. The adjusted GMT ratios between Lot A and Lot B, Lot A and Lot C, and Lot B and C were 0.95; 0.83, and 0.87, respectively.

Overall, pain was the most commonly reported solicited local symptom (83.2% of subjects in the Vaccine Group and 20% of subjects in the Placebo Group). Swelling and redness were reported respectively by 10.4% and 8.5% of subjects in the Vaccine Group, and by 0.7% and 0.7% of subjects in the Placebo Group.

Overall muscle aches were the most commonly reported solicited general symptom (45.2% of subjects in the Vaccine Group and by 20.6% of subjects in the Placebo Group). Headache was reported by 33.3% of subjects in the Vaccine Group and by 27.8% of subjects in the Placebo Group. Fatigue was reported by 32.4% of subjects in the Vaccine Group and by 22.5% of subjects in the Placebo Group. Joint pain at the other location was reported by 25.3% of subjects in the Vaccine Group and by 12.1% of subjects in the Placebo Group. Shivering was reported by 16.7% of subjects in the Vaccine Group and by 9.7% of subjects in the Placebo Group. Sweating was reported by 10.7% of subjects in the Vaccine Group and by 7.3% of subjects in the Placebo Group. Temperature $\geq 38.0^{\circ}\text{C}$ was reported by 4.6% of subjects in the Vaccine Group and by 3.4% of subjects in the Placebo Group.

During the 21-day follow-up period after each vaccination at least one unsolicited AE was reported by 39.7% of subject in the Vaccine Group and by 37.6% of subjects in the Placebo Group for the 18 to 64 years age stratum. These values were

respectively 35.7% and 30.5% for the > 64 years age stratum.

Overall, during the 85 days (Day 0-84) period after the first vaccination at least one unsolicited AE was reported by 44.1% of subject in the Vaccine Group and by 41.8% of subjects in the Placebo Group for the 18 to 64 years age stratum. These values were respectively 41.8% and 35% for the > 64 years age stratum.

Up to Day 182, at least one SAE was reported by 1.0% of subjects in the Vaccine Group and by 0.9% of subjects in the Placebo Group for the 18 to 64 years age stratum. These values were respectively 3.8% and 3.8% for the > 64 years age stratum. Fatal SAEs were reported in 4 subjects in the Vaccine Group (2 in each age stratum) and in 2 subject in the Placebo Group (1 in each age stratum). None of the SAEs were deemed by the investigator to be causally related to vaccination.

Up to Day 182, at least one medically attended AE was reported by 20.8% of subjects in the Vaccine Group and by 20.1% of subjects in the Placebo Group for the 18 to 64 years age stratum. These values were respectively 26.7% and 24.8% for the > 64 years age stratum.

Up to day 379, at least one SAE was reported by 2% of the subjects in both the Vaccine and the Placebo Group for the 18-64 years age stratum. The values were 5.8% and 8.1% for the > 64 years age stratum. Fatal SAEs were reported in 4 subjects in the Vaccine Group (2 in each age stratum) and in 5 subjects in the Placebo Group (1 in the 18-64 age stratum and 4 in the > 64 age stratum). None of the SAEs were assessed by the investigator to be causally related to vaccination.

Up to day 379, at least one medically attended AE was reported by 27.2% of the subjects in the Vaccine Group and 27.6% of the subjects in the Placebo Group for the 18 to 64 years age stratum. These values were 35.8% and 36.1% for the > 64 years age stratum respectively.

Please also refer to the publication below.

Publications:

Langley J et al. AS03-adjuvanted A/Indonesia/5/05 H5N1 pre pandemic vaccine consistently induces strong, broad and persistent immunity in young adults and the elderly. Abstract presented at Infectious Diseases Society of America (IDSA). Philadelphia, Pennsylvania, 29 October-1 November 2009.

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