The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No.: 108251; 108252; 111275, 111276

Title: A phase II, randomised, open study to evaluate the immunogenicity and safety of a single or double-dose of the pandemic influenza candidate vaccine given following a two-administration schedule (21 days apart) in adults over 60 years of age.

Rationale: The present study was designed to evaluate the immunogenicity and safety of a single or double dose of pandemic influenza (H5N1) vaccine, for healthy adults over 60 years of age. Subjects who had not been vaccinated with an influenza vaccine for the 2006-2007 season received *Fluarix*[™] at least 3 weeks before administration of the first dose(s) of the H5N1 vaccine. The persistence of H5N1 influenza antibodies was also evaluated up to two years after vaccination. H5N1 vaccine: GlaxoSmithKline (GSK) Biologicals' pandemic monovalent influenza vaccine.

Fluarix[™] (Flu): GSK Biologicals' seasonal influenza split vaccine

Phase: II

Study Period:

108251: 17 November 2006 to 27 October 2007.

108252: 14 June 2007 to 05 March 2008.

111275: 06 March 2008 to 12 September 2008

111276: 09 March 2009 to 14 September 2009

Study Design: Multi-centre, randomised (3:1:3:1), open study with 4 groups.

Data from the group receiving the currently registered vaccine are presented. Data from the investigational vaccination regimens, which are not approved or marketed, are not reported.

Centres:

108251 & 108252: 12 study centres: 7 in Belgium and 5 in Italy.

111275 & 111276: 7 study centres in Belgium.

Indication: Immunisation against influenza disease during a pandemic in subjects over 60 years of age.

Treatment: All subjects received 2 administrations of the vaccine. The study groups were as follows:

- 2 groups received investigational H5N1 formulations.
- H5N1 Group: received a single dose of H5N1 vaccine intramuscularly in the deltoid region of the non-dominant arm at Days 0 and 21.
- Double H5N1 Group: received a double dose of H5N1 vaccine intramuscularly in the deltoid region of each arm at Days 0 and 21

Subjects not previously vaccinated with an influenza vaccine for the 2006-2007 season were administered Flu vaccine intramuscularly at least 3 weeks before administration of the first dose(s) of the H5N1 vaccine.

Objectives:

Only objectives related to the licensed vaccine are presented.

- To evaluate the immunogenicity of the H5N1 vaccine administered as a single or double dose in terms of humoral immune response 21 days after the first and second vaccination (for anti-haemagglutinin [anti-HA] antibody response) and 21 days after the second vaccination (for neutralising antibody response).
- To assess the persistence of antibodies 180 days, one year and two years after the first vaccination with the H5N1 vaccine.

Primary Outcome/Efficacy Variable:

Only outcome variables related to the licensed vaccine are presented.

Immunogenicity

For the humoral immune response in terms of H5N1 haemagglutination-inhibition (HI) antibodies, the following parameters (with 95% confidence intervals [CIs]) were calculated:

- Geometric mean titres (GMTs) of H5N1 antibody titres at Days 0, 21, 42 and 180 for all subjects and in addition, Month 12 and Month 24 for subjects in Belgium.
- Seroconversion rates* (SCR) at Days 21, 42 and 180 for all subjects and in addition, Month 12 and Month 24 for subjects in Belgium.
- Seroconversion factors** (SCF) at Days 21, 42 and 180 for all subjects and in addition, Month 12 and Month 24 for subjects in Belgium.
- Seroprotection rates*** (SPR) at Days 0, 21, 42 and 180 for all subjects and in addition, Month 12 and Month 24 for subjects in Belgium.

In addition, humoral immune response in terms of neutralising antibodies was evaluated in a subset of subjects using the following parameters (with 95% CIs):

- GMTs of H5N1 antibody titres at Days 0, 42 and 180 and in addition, Month 12 and Month 24 for subjects in Belgium.
- SCR*§ at Days 42 and 180 and in addition, Month 12 and Month 24 for subjects in Belgium.

* SCR for H5N1 HI antibodies response was defined as the percentage of vaccinees who had either a pre-vaccination titre < 1:10 and a post-vaccination titre \geq 1:40 or a pre-vaccination titre \geq 1:10 and at least a 4-fold increase in post-vaccination titre.

**SCF was defined as the fold increase in serum H5N1 HI antibodies GMTs post-vaccination compared to Day 0.

***SPR was defined as the percentage of vaccinees with a serum H5N1 HI antibodies titre \geq 1:40 that usually was accepted as indicating protection.

[§] SCR for neutralising antibody response was defined as the percentage of vaccinees with a minimum 4-fold increase in neutralising antibody titre at post-vaccination.

Secondary Outcome/Efficacy Variables:

Only outcome variables related to the licensed vaccine are presented. Safety

- Percentage, intensity and relationship to vaccination of solicited local and general signs and symptoms during a 7day follow-up period (Day 0-6) after each dose of the H5N1 vaccine and overall.
- Percentage, intensity and relationship to vaccination of unsolicited local and general signs and symptoms during the 21 days following the first vaccination with the H5N1 vaccine (Day 0-20) and during the 30 days following the second vaccination (Day 0-29).
- Occurrence of serious adverse events (SAEs) during the entire study period.
- Occurrence of adverse events of specific interest (AESIs) during the entire study (for subjects in Belgium).
- Number and percentage of subjects with normal or abnormal values at each scheduled time point (Day 0, Day 2, Day 21, Day 23), for biochemical assessments and for haematological analysis.

Immunogenicity

For the cell-mediated immunity (CMI) response evaluation:

The following parameters (with 95% CIs) were calculated at Days 0, 21, 42 and 180 for all subjects and in addition, Month 12 and Month 24 for subjects in Belgium:

- Frequency of influenza-specific Cluster of Differentiation (CD) 4/CD8 T-cells per 10⁶ in tests producing at least two different cytokines (CD40 ligand [CD40L], interleukin-2 [IL-2], tumour necrosis factor-alpha [TNF-α], interferongamma [IFN-γ]).
- Frequency of influenza-specific CD4/CD8 T-cells per 10⁶ in tests producing at least CD40L and another signal molecule (IL-2, IFN-γ, TNF-α).
- Frequency of influenza-specific CD4/CD8 T-cells per 10⁶ in tests producing at least IL-2 and another signal molecule (CD40L, IFN-γ, TNF-α).
- Frequency of influenza-specific CD4/CD8 T-cells per 10⁶ in tests producing at least TNF-α and another signal molecule (IL-2, IFN-γ, CD40L).
- Frequency of influenza-specific CD4/CD8 T-cells per 10⁶ in tests producing at least IFN-γ and another signal molecule (CD40L, IL-2, TNF-α).

Statistical Methods:

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

- The Total Vaccinated Cohort included all vaccinated subjects for whom data were available.
- The ATP cohort for immunogenicity included all evaluable subjects (i.e., those meeting all eligibility criteria, complying
 with the procedures defined in the protocol, with no elimination criteria during the study) for whom immunogenicity data
 were available. This included all subjects for whom assay results for antibodies against at least one study vaccine
 antigen component after vaccination were available.
- The ATP cohort for persistence included all evaluable subjects who met all eligibility criteria, who complied with the protocol procedures during the entire study period and with the intervals defined in the protocol at Day 180, at Month 12 and at Month 24, who did not meet the elimination criteria during the study, for whom data concerning persistence outcome variable measures were available. This included all subjects for whom assay results for antibodies against at least one study vaccine antigen component at Day 180, at Month 12 and at Month 24 were available.

Analysis of immunogenicity:

The analysis was performed on the ATP cohort for immunogenicity and the ATP cohort for persistence.

Descriptive analysis:

For the humoral immune response in terms of H5N1 HI antibodies, the GMTs of H5N1 HI antibodies and SPR at Days 0, 21, 42, 180 for all subjects and Months 12 and 24, for subjects in Belgium, the SCR and SCF at Days 21, 42, 180 for all subjects and Months 12 and 24, for subjects in Belgium with their 95% CIs were calculated for each group. For the humoral immune response in terms of neutralising antibodies, the GMTs of H5N1 HI antibodies at Days 0, 42, 180 for all subjects and Months 12 & 24 for subjects in Belgium and SCR at Days 42, 180 for all subjects and Months 12 & 24 for subjects in Belgium and SCR at Days 42, 180 for all subjects and Months 12 & 24 for subjects in Belgium and SCR at Days 42, 180 for all subjects and Months 12 & 24 for subjects in Belgium and SCR at Days 42, 180 for all subjects and Months 12 & 24 for subjects in Belgium and SCR at Days 6. In the subject of the assay were given an arbitrary value of half the cut-off for the purpose of GMT calculation. The frequency of influenza-specific CD4/CD8 T lymphocytes cells was summarised (descriptive statistics) for each vaccine group at Days 0, 21, 42, 180 for all subjects and Months 12 and 24 for subjects in Belgium.

Analysis of safety

The analysis was based on the Total Vaccinated Cohort.

The percentage of subjects reporting each individual solicited local and general symptom during the 7-day (Day 0-6) solicited follow-up period was tabulated with exact 95% CI. The same tabulation was performed for grade 3 symptoms and for general symptoms with relationship to vaccination. The number and proportion of subjects with normal or abnormal values for each haematology and biochemistry parameter was tabulated for each study group at each scheduled time point. The proportion of subjects with at least one report of unsolicited adverse event (AE) classified by the Medical Dictionary for Regulatory Activities (MedDRA) preferred terms and reported up to 21 days after the first vaccination with H5N1 vaccine and 30 days after the second vaccination was tabulated. The same tabulation was performed for grade 3 AEs and for AEs with a relationship to vaccination. The occurrence of SAEs and AESIs during the study period (up to Month 24) was tabulated according to MedDRA preferred terms.

Study Population: Healthy male or female subjects aged 61 years and above at the time of first vaccination were enrolled in the study. Written informed consent was obtained from the subjects prior to study entry.

Number of Subjects:	H5N1 Group	Double H5N1 Group
Primary study – Day 51 (108251)		
Planned, N	180	180
Randomised, N (Total Vaccinated Cohort)	165	159
Completed, n (%)	158 (96.0)	153 (96.2)
Total Number Subjects Withdrawn, n (%)	7 (4.2)	6 (3.8)
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 (%)	7 (4.2)	6 (3.8)
Demographics	H5N1 Group	Double H5N1 Group
N,(Total Vaccinated Cohort)	165	159
Females: Males	72:93	77:82
Mean Age, years (SD)	69.7 (6.33)	69.7 (6.51)
White-Caucasian/European heritage, n (%)	163 (98.8)	151 (95.0)
Day 180 (108252)		
Number of subjects	H5N1 Group	Double H5N1 Group
Planned, N	164	158
Entered, N (Total Vaccinated Cohort)	164	158
Completed, n (%)	162 (98.8)	153 (96.8)
Total Number Subjects Withdrawn, n (%)	2 (1.2)	5 (3.2)
Withdrawn due to Adverse Events, n (%)	0 (0.0)	2 (1.3)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	2 (1.2)	3 (1.9)
Demographics	H5N1 Group	Double H5N1 Group
N (Total Vaccinated Cohort)	164	158
Females: Males	72:92	74:84
Mean Age, years (SD)	69.7 (6.37)	69.6 (6.54)
Missing race, n (%)	164 (100)	158 (100)
Month 12 (111275)		
Number of subjects	H5N1 Group	Double H5N1 Group

Planned, N						125					
Entered, N (Total Vaccinat	ed Coho	ort)			130			125		
Completed, r	า (%)				13	0 (100)		1:	25 (100)		
Total Numbe	er Subjects Wit	hdrawn,	n (%)		C) (0.0)			0 (0.0)		
Withdrawn d	ue to Adverse	Events,	n (%)		C	0.0)			0 (0.0)		
Withdrawn d	ue to Lack of I	Efficacy,	n (%)		Not a	applicable		Not	applicable		
Withdrawn fo	or other reasor	ıs, n (%)			C	0.0)		0 (0.0)			
Demograph	ics				H5N		Double H5N1 Group				
N (Total Vac	cinated Cohor	t)				130		125			
Females: Ma	ales				Į	58:72			63:62		
Mean Age, y	ears (SD)				69.	4 (6.67)		69	0.5 (6.43)		
White - Cauc	asian / Europ	ean heri	tage, n (S	%)	12	8 (98.5)		1′	18 (94.4)		
Month 24 (1	Month 24 (111276)										
Number of s	subjects				H5N	1 Group		Double	H5N1 Gr	oup	
Planned, N						122			117		
Entered, N (Total Vaccinat	ed Coho	ort)			122			117		
Completed, r	n (%)				12	2 (100)		1	17 (100)		
Total Numbe	er Subjects Wit	hdrawn,	n (%)		C	0.0)			0 (0.0)		
Withdrawn d	ue to Adverse	Events,	n (%)		C	0.0)			0 (0.0)		
Withdrawn d	ue to Lack of I	Efficacy,	n (%)		Not a	applicable		Not	applicable		
Withdrawn fo	or other reasor	ıs, n (%)			C	0.0)			0 (0.0)		
Demograph	ics				H5N	1 Group		Double	H5N1 Gr	oup	
N (Total Vac	cinated Cohor	t)				122			117		
Females: Ma	ales				Į	54:68			62:55		
Mean Age, y	ears (SD)				69.	5 (6.76)		69	0.3 (6.48)		
White - Cauc	asian / Europ	ean heri	tage, n (S	%)	12	0 (98.4)		1′	10 (94.0)		
Primary Out	come/Efficac	v Varial	ala: Soro	nocitivity	rates and GN	ITs of H5N1	HI antibodie	dies against the vaccine strain			
1 mary Out		y variai	Jie. Seit	positivity	vity rates and GMTs of H5N1 HI antibodies against the vaccine strain nicity)						
A/Vietnam/1	194/2004 (ATF	cohort	for immu	inogenici	ty)			is against the		uan	
A/Vietnam/17 Group	194/2004 (ATF Timing	cohort N	for immu	inogenici	ty) _≥ 1: 10			G	MT	uan	
A/Vietnam/11	194/2004 (ATF	^P cohort N	for immu	inogenici	ty) ≥ 1: 10	95% CI	va	G Ilue	MT 95%		
A/Vietnam/1 ² Group	194/2004 (ATF	² cohort N	for immu	inogenicit	ty) ≥ 1: 10 LL	05% CI	va	G	MT 95% LL		
A/Vietnam/11 Group H5N1	194/2004 (ATF Timing PRE	^o cohort N 152	n 62	40.8	ty) ≥ 1: 10 LL 32.9	05% CI UL 49.0	va 1	G	MT 95% LL 9.2	CI UL 13.9	
A/Vietnam/11 Group H5N1	194/2004 (ATF Timing PRE PI(D21)	2 cohort N 152 152	n 62 122	40.8 80.3	2 1: 10 2 1: 10 2 1: 10 2 1: 10 2 1: 10 32.9 73.0	95% CI UL 49.0 86.3	va 1 5	G	MT 95% LL 9.2 38.1	CI UL 13.9 65.6	
A/Vietnam/11 Group H5N1	194/2004 (ATF Timing PRE PI(D21) PII(D42)	2 cohort N 152 152 152	n 62 122 142	40.8 80.3 93.4	ty) ≥ 1: 10 LL 32.9 73.0 88.2	95% CI UL 49.0 86.3 96.8	va 1 50 12	G lue 1.3 0.0 26.8	MT 95% LL 9.2 38.1 99.4	CI UL 13.9 65.6 161.7	
A/Vietnam/1 ⁺ Group H5N1 Double	194/2004 (ATF Timing PRE PI(D21) PII(D42) PRE	2 cohort N 152 152 152 152 145	n 62 122 142 52	40.8 80.3 93.4 35.9	ty) ≥ 1: 10 LL 32.9 73.0 88.2 28.1	05% CI UL 49.0 86.3 96.8 44.2	va 1 50 12	G lue 1.3 0.0 16.8 0.2	MT 95% LL 9.2 38.1 99.4 8.4	CI UL 13.9 65.6 161.7 12.5	
A/Vietnam/11 Group H5N1 Double H5N1	PRE PI(D21) PII(D42) PRE PI(D21)	2 cohort N 152 152 152 145 145	n 62 122 142 52 130	40.8 40.8 80.3 93.4 35.9 89.7	LL 32.9 73.0 88.2 28.1 83.5	95% CI UL 49.0 86.3 96.8 44.2 94.1	va 1 50 12 10 10	G Ilue 1.3 0.0 16.8 0.2 9.4	MT 95% LL 9.2 38.1 99.4 8.4 52.1	CI UL 13.9 65.6 161.7 12.5 92.3	
A/Vietnam/11 Group H5N1 Double H5N1	PRE PI(D21) PII(D42) PRE PI(D21) PII(D42) PRE PI(D21)	2 cohort N 152 152 152 145 145 145	n 62 122 142 52 130 142	40.8 40.8 80.3 93.4 35.9 89.7 97.9	LL 32.9 73.0 88.2 28.1 83.5 94.1	95% CI UL 49.0 86.3 96.8 44.2 94.1 99.6	va 1 12 12 10 69 23	G Ilue 1.3 0.0 26.8 0.2 9.4 57.3	MT 95% LL 9.2 38.1 99.4 8.4 52.1 191.9	CI UL 13.9 65.6 161.7 12.5 92.3 293.6	
A/Vietnam/11 Group H5N1 Double H5N1 GMT = Geon	PRE PI(D21) PII(D42) PRE PI(D21) PII(D42) PII(D42) netric mean an	2 cohort N 152 152 152 145 145 145 145 145	n 62 122 142 52 130 142 itre	40.8 40.8 80.3 93.4 35.9 89.7 97.9	LL 32.9 73.0 88.2 28.1 83.5 94.1	95% CI UL 49.0 86.3 96.8 44.2 94.1 99.6	va 1 12 12 11 60 23	G Ilue 1.3 0.0 26.8 0.2 9.4 17.3	MT 95% LL 9.2 38.1 99.4 8.4 52.1 191.9 1 1	CI UL 13.9 65.6 161.7 12.5 92.3 293.6	
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	2) 1/	15	108	74.5	6	6.6	<u>81</u> /		24	1	10.0	30.0
GMT = Geometric mea	n antibody tit	то —	100	74.5		0.0	01.4		24.	Ŧ	15.5	50.0
N = number of subjects	with availabl	e results										
n (%) = number (nerce)	ntage) of subi	iects with	titre withi	n the sne	cified ra	ande						
95% CI = 95% confider	nce interval. I		r Limit [.] U	I = Unnet	er I imit	ungo						
PRF = Pre-vaccination	at Day 0		i Linit, O									
PI (D21) = Post-vaccin	ation at Day 2	01										
PII (D42) = Post-vaccin	ation at Day	42										
Primary Outcome/Eff	icacy Variabl	e Serono	ositivity ra	tes and	GMTso	f H5N1 F	-II antibo	dies a	nainst	A/Vietn	am/1194	/2004
and A/Indonesia/05/20	05 strains at I	Day () and	Dav 180	(ATP co	bort for	persiste	nce at D	av 18	(gainet ())	/ • • • • • • •		/2001
Antibodies against	Group	Tim	nina	N		>	1: 10		•/		GMT	
·					n	%	95	% CI		value	95%	
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		PF	RE	142	58	40.8	32.7	40	-	11.6	94	14.3
	H5N1	PII/D	180)	140	107	76.4	68.5	83	12	38.5	30.0	49.5
A/Vietnam/1194/2004	Double	PF	7100) RF	135	48	35.6	27.5	44	.2	10.0	82	12.3
	H5N1		180)	131	113	86.3	70.2	01	6	53.5	/1 0	68.4
				1/12	3	2.1	0.4	6	0	51	50	5.2
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A/Indonesia/5/2005	Doublo			125	20	∠1.4))	14.3 Λ κ	23 6	1	5.0	5.0	5.2
			NE 11201	133	5	Z.Z /1 0	22.7	50	.4	9.1	7.5	0.0
GMT = Geometrie maa	n antibody tit	 ro	/100)	IJ	J 4	דו.2	52.1	50	·. ∠	0.0	i.J	9.9
N - Number of subject	n antibuuy titi s with availab	le reculte										
n/0/2 = number/percents	s will availab	citivo cubi	iocte (HI t	itro > 1·	10)							
95% CI = $95%$ confider	age of seropo		r Limit II	.ut ⊂ 1. I – ∐nnv	ar Limit							
PRF = Pre vaccination	at Day 0	L - LOWE	i Linit, U									
PII(D180) = Post-vacci	nation at Day	180										
1 11(0100) 1 000 1000	nation at Day	100										
Primary Outcome/Efficacy Variable: Seronositivity rates and GMTs of H5N1 HI antibodies against A/Vietnam/1194/2004												
Primary Outcome/Effi	icacy Variabl	e: Seropo Dav 0 and	ositivity ra Month 1	tes and 2 (ATP c	GMTs o ohort fo	f H5N1 H r persist	I antibo	dies a Month	igainst 12)	A/Vietn	am/1194	/2004
Primary Outcome/Effi and A/Indonesia/05/20	i cacy Variabl 05 strains at [e: Seropo Day 0 and	ositivity ra Month 1	tes and 2 (ATP c	GMTs o ohort fo	f H5N1 ⊦ r persiste ≤	H antibo ence at I ≥ 1: 10	dies a Nonth	igainst 12)	A/Vietn	am/1194 GMT	/2004
Primary Outcome/Effi and A/Indonesia/05/20 Antibodies against	icacy Variabl	e: Seropo Day 0 and Timing	ositivity ra I Month 1	tes and 2 (ATP c	GMTs o ohort fo	f H5N1 ⊦ r persiste ≥	H antibo ence at I ≥ 1: 10	dies a Month 95% C	igainst 12) Cl	A/Vietn	am/1194 GMT 95%	/2004 % Cl
Primary Outcome/Effi and A/Indonesia/05/20 Antibodies against	icacy Variabl 05 strains at I Group	e: Seropo Day 0 and Timing	ositivity ra I Month 1	tes and 2 (ATP c N	GMTs o cohort fo n	f H5N1 ⊦ r persistr ≥ %	H antibo ence at l ≥ 1: 10 LL	dies a Month 95% C	igainst 12) CI	A/Vietn value	am/1194 GMT 95%	/2004 % CI
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GMT = Geometric mean antibody titre

N = Number of subjects with available results

n (%)= number (percentage) of seropositive subjects (HI titre \ge 1:10)

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

PRE = Pre-vaccination on Day 0

PII(M12)= Post-vaccination 2 at Month 12

PII(M24)= Post-vaccination 2 at Month 24

Primary Outcome/Efficacy Variable: SCR for H5N1 HI antibodies against A/Vietnam /1194/2004 and A/Indonesia/5/2005 strains at each post-vaccination at Day 21 and Day 42 (ATP cohort for immunogenicity)

Antibodies against	Group	Timing	Ν		S	CR	
				n	%	9	5% CI
						LL	UL
	H5N1	PI(D21)	152	69	45.4	37.3	53.7
A/Viotnom/1104/2004		PII(D42)	152	110	72.4	64.5	79.3
A/VIELIIdiii/1154/2004	Double	PI(D21)	145	76	52.4	44.0	60.8
	H5N1	PII(D42)	145	128	88.3	81.9	93.0
	H5N1	PI(D21)	152	5	3.3	1.1	7.5
A/Indonesia/5/2005		PII(D42)	152	35	23.0	16.6	30.5
A/Indonesia/5/2005	Double	PI(D21)	145	13	9.0	4.9	14.8
	H5N1	PII(D42)	145	58	40.0	32.0	48.5

N = number of subjects with available results

n (%) =number (percentage) of subjects with either a pre-vaccination titre <1:10 and post-vaccination titre \geq 1:40 or a pre-vaccination titre \geq 1:10 and a minimum 4-fold increase in post-vaccination titre

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

PI(D21) = Post vaccination at Day 21

PII(D42) =Post vaccination at Day 42

Primary Outcome/Efficacy Variable: SCR for H5N1 HI antibodies against A/Vietnam /1194/2004 and A/Indonesia/5/2005 strains at post-vaccination Day 180 (ATP cohort for persistence at Day 180)

Antibodies against	Group	Timing	Ν		S	CR	
				n	%	959	% CI
						LL	UL
A Wistner /1104/2004	H5N1	PII(D180)	140	52	37.1	29.1	45.7
A/vietnam/1194/2004	Double H5N1	PII(D180)	130	70	53.8	44.9	62.6
A/Indonesia/E/200E	H5N1	PII(D180)	140	5	3.6	1.2	8.1
A/Indonesia/5/2005	Double H5N1	PII(D180)	130	8	62	27	11.8

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

PII(D180) = Post-vaccination at Day 180

Primary Outcome/Efficacy Variable: SCR for H5N1 HI antibodies against A/Vietnam /1194/2004 and A/Indonesia/5/2005 strains at post-vaccination Month 12 (ATP cohort for persistence at Month 12)

Antibodies against	Group	Timing	N		SCR		
				n	%	95%	6 CI
						LL	UL
A/Vietnam/1194/2004	H5N1	PII(M12)	112	24	21.4	14.2	30.2
	Double H5N1	PII(M12)	105	24	22.9	15.2	32.1
A/Indonesia/5/2005	H5N1	PII(M12)	112	17	15.2	9.1	23.2
	Double H5N1	PII(M12)	105	22	21.0	13.6	30.0

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

PII(M12) = Post-vaccination at Month 12

Primary Outcome/Efficacy Variable: SCR for H5N1 HI antibody titres against A/Vietnam/1194/2004 strains and A/Indonesia/05/2005 at Month 24 (ATP cohort for persistence at Month 24)

Antibodies against	Group	Timing	Ν			SCR	
				n	%	95	5% CI
						LL	UL
A/Vietnam/1194/2004	H5N1	PII(M24)	86	8	9.3	4.1	17.5
	Double H5N1	PII(M24)	81	9	11.1	5.2	20.0
A/Indonesia/5/2005	H5N1	PII(M24)	86	4	4.7	1.3	11.5
	Double H5N1	PII(M24)	81	4	4.9	1.4	12.2

Seroconversion defined as:

For initially seronegative subjects, antibody titre ≥ 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

PRE = Pre-vaccination at Day 0

PII(M12)= Post-vaccination 2 at Month 12

PII(M24)= Post-vaccination 2 at Month 24

Primary Outcome/Efficacy Variable: SCF for H5N1 HI antibodies against A/Vietnam/1194/2004 and A/Indonesia/5/2005 strain (ATP cohort for immunogenicity)

Antibodies against	Group	Timing	Ν		SCF	
				Value	95%	CI
					LL	UL
	H5N1	PI(D21)	152	4.4	3.5	5.5
A/Vietnam/1194/2004		PII(D42)	152	11.2	8.9	14.1
A/Vietilaini/1194/2004	Double	PI(D21)	145	6.8	5.3	8.6
	H5N1	PII(D42)	145	23.2	18.5	29.0
	H5N1	PI(D21)	152	1.4	1.2	1.5
Alladonosia/5/2005		PII(D42)	152	2.7	2.2	3.2
AIIIUUIIESId/J/200J	Double	PI(D21)	145	1.7	1.4	2.0
	H5N1	PII(D42)	145	4.8	3.9	5.9

N = number of subjects with available results

SCF = Seroconversion Factor or geometric mean ratio (mean[log10(POST/PRE)])

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

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

PRE =Pre-vaccination at Day 0

PI(D21) = Post vaccination at Day 21

PII(D42) = Post vaccination at Day 42

Primary Outcome/Efficacy Variable: SCF for H5N1 HI antibodies against A/Vietnam/1194/2004 and A/Indonesia/5/2005 strains at post-vaccination Day 180 (ATP cohort for persistence at Day 180)

Antibodies against	Group	Timing	N	SCF		
				Value	95%	CI
					LL	UL
A/Vietnem/1101/2001	H5N1	PII(D180)	140	3.3	2.7	4.0
A/Vietilalii/1194/2004	Double H5N1	PII(D180)	130	5.4	4.4	6.7
Alladonooio/5/2005	H5N1	PII(D180)	140	1.3	1.2	1.4
A/Indonesia/5/2005	Double H5N1	PII(D180)	130	1.7	1.5	1.9

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

PII(D180) = Post-vaccination at Day 180

Primary Outcome/Efficacy Variable: SCF for H5N1 HI antibodies against A/Vietnam/1194/2004 and A/Indonesia/5/2005

strains at post-vaccina	tion Month 12 (ATP	cohort for persiste	nce at Mo	nth 12)						
Antibodies against	Group	Timing		Ν		SCF				
					Value		95%	CI		
						LL		UL		
A/Vietnam/1194/2004	H5N1	PII(M12)		112	1.8	1.5		2.2		
	Double H5N1	PII(M12)		105	2.5	2.0		3.0		
A/Indonesia/5/2005	H5N1	PII(M12)		112	1.9	1.6		2.3		
	Double H5N1	PII(M12)		105	2.6	2.2		3.1		
N = Number of subjects SCF = Seroconversion 95% CI = 95% confiden PII(M12) = Post-vaccina Primary Outcome/Effi	Factor or geometric Factor or geometric Ice interval, LL = Low ation at Month 12 Cacy Variable: SCF	vaccination results mean ratio (mean ver Limit, UL = Up for H5N1 HI antib	available [log10(POS per Limit	ST/PRE)])	Vietnam /119	4/2004 and				
A/Indonesia/05/2005 st	rains at Month 24 (A	TP cohort for pers	istence at l	Month 24)	1/200 T 4110				
Antibodies against	Group	Timing		Ν		SCF				
	-				Value		95% C			
						LL		UL		
A/Vietnam/1194/200	H5N1	PII(M24)		86	1.5	1.3		1.8		
4	Double H5N1	PII(M24)		81	1.9	1.6		2.3		
A/Indonesia/5/2005	H5N1	PII(M24)		86	1.4	1.2		1.6		
	Double H5N1	PII(M24)		81	1.4	1.2		1.7		
N = Number of subjects with pre- and post-vaccination results available SCF = Seroconversion factor or geometric mean ratio (mean[log ₁₀ (POST/PRE)]) 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PII(M12)= Post-vaccination 2 at Month 12 PII(M24)= Post-vaccination 2 at Month 24 Primary Outcome/Efficacy Variable: SPR for H5N1 HI antibodies against A/Vietnam/1194/2004 and A/Indonesia/5/2005										
	Group	Timina	N			SPR				
Antiboales against	Group	Timing	N	n	%	SPR	95% (
Antibouleo uguinot	Group	Timing	N	n	%	SPR	95% C	CI UL		
	H5N1	Timing	N 152	n 28	% 18.4	SPR LL 12.6	95% 0	CI UL 25.5		
	H5N1	Timing PRE PI(D21)	N 152 152	n 28 93	% 18.4 61.2	SPR LL 12.6 53.0	95% C	UL 25.5 69.0		
	H5N1	PRE PI(D21) PII(D42)	N 152 152 152	n 28 93 127	% 18.4 61.2 83.6	SPR LL 12.6 53.0 76.7	95% C	UL 25.5 69.0 89.1		
A/Vietnam/1194/2004	H5N1 Double H5N1	PRE PI(D21) PII(D42) PRE	N 152 152 152 145	n 28 93 127 23	% 18.4 61.2 83.6 15.9	SPR LL 12.6 53.0 76.7 10.3	95% C	UL 25.5 69.0 89.1 22.8		
A/Vietnam/1194/2004	H5N1 Double H5N1	PRE PI(D21) PII(D42) PRE PI(D21)	N 152 152 152 152 145 145	n 28 93 127 23 90	% 18.4 61.2 83.6 15.9 62.1	SPR LL 12.6 53.0 76.7 10.3 53.6	95% (UL 25.5 69.0 89.1 22.8 70.0		
A/Vietnam/1194/2004	H5N1 Double H5N1	PRE PI(D21) PII(D42) PRE PI(D21) PII(D42) PRE PI(D21) PII(D42)	N 152 152 152 145 145 145	n 28 93 127 23 90 139	% 18.4 61.2 83.6 15.9 62.1 95.9	SPR LL 12.6 53.0 76.7 10.3 53.6 91.2	95% C	UL 25.5 69.0 89.1 22.8 70.0 98.5		
A/Vietnam/1194/2004	Group H5N1 Double H5N1 H5N1	PRE PI(D21) PII(D42) PRE PI(D21) PIE PI(D21) PRE PI(D21) PIE PII(D42) PRE	N 152 152 152 145 145 145 145 152	n 28 93 127 23 90 139 0	% 18.4 61.2 83.6 15.9 62.1 95.9 0.0	SPR LL 12.6 53.0 76.7 10.3 53.6 91.2 0.0	95% (UL 25.5 69.0 89.1 22.8 70.0 98.5 2.4		
A/Vietnam/1194/2004	Group H5N1 Double H5N1 H5N1	PRE PI(D21) PII(D42) PRE PI(D21) PII(D42) PRE PI(D21) PII(D42) PII(D42) PII(D42) PII(D42) PII(D42) PII(D42) PII(D42)	N 152 152 152 145 145 145 145 152 152	n 28 93 127 23 90 139 0 5	% 18.4 61.2 83.6 15.9 62.1 95.9 0.0 3.3	SPR LL 12.6 53.0 76.7 10.3 53.6 91.2 0.0 1.1	95% (UL 25.5 69.0 89.1 22.8 70.0 98.5 2.4 7.5		
A/Vietnam/1194/2004	Group H5N1 Double H5N1 H5N1	PRE PI(D21) PII(D42)	N 152 152 152 145 145 145 145 152 152	n 28 93 127 23 90 139 0 5 35	% 18.4 61.2 83.6 15.9 62.1 95.9 0.0 3.3 23.0	SPR LL 12.6 53.0 76.7 10.3 53.6 91.2 0.0 1.1 16.6	95% (UL 25.5 69.0 89.1 22.8 70.0 98.5 2.4 7.5 30.5		
A/Vietnam/1194/2004 A/Indonesia/5/2005	Group H5N1 Double H5N1 H5N1 Double H5N1	Timing PRE PI(D21) PII(D42) PRE PI(D21) PII(D42) PRE PI(D21) PII(D42) PRE PI(D21) PRE PI(D21) PRE PI(D21) PRE PI(D21) PRE PI(D21) PII(D42) PRE	N 152 152 152 145 145 145 152 152 152 152 152 145	n 28 93 127 23 90 139 0 5 35 35 0	% 18.4 61.2 83.6 15.9 62.1 95.9 0.0 3.3 23.0 0.0	SPR LL 12.6 53.0 76.7 10.3 53.6 91.2 0.0 1.1 16.6 0.0	95% (UL 25.5 69.0 89.1 22.8 70.0 98.5 2.4 7.5 30.5 2.5		
A/Vietnam/1194/2004 A/Indonesia/5/2005	Group H5N1 Double H5N1 H5N1 Double H5N1	PRE PI(D21) PII(D42) PRE PI(D21)	N 152 152 145 145 145 145 152 152 152 152 152 145 145	n 28 93 127 23 90 139 0 5 35 0 13	% 18.4 61.2 83.6 15.9 62.1 95.9 0.0 3.3 23.0 0.0 9.0	SPR LL 12.6 53.0 76.7 10.3 53.6 91.2 0.0 1.1 16.6 0.0 4.9	95% (UL 25.5 69.0 89.1 22.8 70.0 98.5 2.4 7.5 30.5 2.5 14.8		
A/Vietnam/1194/2004	Group H5N1 Double H5N1 H5N1 Double H5N1	PRE PI(D21) PII(D42) PRE PII(D42) PRE PI(D21) PII(D42) PII(D42)	N 152 152 152 145 145 145 152 152 152 152 145 145 145	n 28 93 127 23 90 139 0 139 0 5 35 0 13 59	% 18.4 61.2 83.6 15.9 62.1 95.9 0.0 3.3 23.0 0.0 9.0 40.7	SPR LL 12.6 53.0 76.7 10.3 53.6 91.2 0.0 1.1 16.6 0.0 4.9 32.6	95% (UL 25.5 69.0 89.1 22.8 70.0 98.5 2.4 7.5 30.5 2.5 14.8 49.2		
A/Vietnam/1194/2004 A/Vietnam/1194/2004 A/Indonesia/5/2005 N = number of subjects n (%) = number (percer 95% CI = 95% confiden PRE =Pre-vaccination PI(D21) = Post vaccina PII(D42) = Post vaccina	Group H5N1 Double H5N1 Double H5N1 Double H5N1 Double H5N1 intage) of subjects with available result intage) of subjects with a content of subjects with a c	PRE PI(D21) PII(D42) St th titre within the s ver Limit, UL= Upp	N 152 152 152 145 145 145 145 152 152 152 145 145 145 145 145 145 145 145	n 28 93 127 23 90 139 0 5 35 0 13 59 nge	% 18.4 61.2 83.6 15.9 62.1 95.9 0.0 3.3 23.0 0.0 9.0 40.7	SPR LL 12.6 53.0 76.7 10.3 53.6 91.2 0.0 1.1 16.6 0.0 4.9 32.6	95% (UL 25.5 69.0 89.1 22.8 70.0 98.5 2.4 7.5 30.5 2.5 14.8 49.2		
A/Vietnam/1194/2004 A/Vietnam/1194/2004 A/Indonesia/5/2005 N = number of subjects n (%) = number (percer 95% CI = 95% confiden PRE =Pre-vaccination PI(D21) = Post vaccina PII(D42) = Post vaccina Primary Outcome/Effi	Group H5N1 Double H5N1 Double H5N1 Double H5N1 Double H5N1 intage) of subjects wi ince interval, LL= Low at Day 0 tion at Day 21 ation at Day 42 cacy Variable: SPR	PRE PI(D21) PII(D42) PRE PI(D21) PII(D42) PRE PI(D21) PII(D42) PRE PI(D21) PII(D42) State th titre within the s /er Limit, UL= Upp	N 152 152 152 145 145 145 145 152 152 152 145 145 145 145 145 145 145 0dies agai	n 28 93 127 23 90 139 0 5 35 0 13 59 13 59 nge	% 18.4 61.2 83.6 15.9 62.1 95.9 0.0 3.3 23.0 0.0 9.0 40.7	SPR LL 12.6 53.0 76.7 10.3 53.6 91.2 0.0 1.1 16.6 0.0 4.9 32.6	95% C	UL 25.5 69.0 89.1 22.8 70.0 98.5 2.4 7.5 30.5 2.5 14.8 49.2 a/5/2005		
A/Vietnam/1194/2004 A/Vietnam/1194/2004 A/Indonesia/5/2005 N = number of subjects n (%) = number (percer 95% CI = 95% confiden PRE =Pre-vaccination PI(D21) = Post vaccina PII(D42) = Post vaccina PII(D42) = Post vaccina	Group H5N1 Double H5N1 Double H5N1 Double H5N1 Double H5N1 ition at Day 21 ition at Day 42 cacy Variable: SPR y 180 (ATP cohort f	PRE PI(D21) PII(D42) St th titre within the s ver Limit, UL= Upp for H5N1 HI antib persistence at D	N 152 152 152 145 145 145 145 152 152 152 145 145 145 145 145 145 145 145	n 28 93 127 23 90 139 0 55 35 0 13 59 nge	% 18.4 61.2 83.6 15.9 62.1 95.9 0.0 3.3 23.0 0.0 9.0 40.7 nam/1194/20	SPR LL 12.6 53.0 76.7 10.3 53.6 91.2 0.0 1.1 16.6 0.0 4.9 32.6	95% C	UL 25.5 69.0 89.1 22.8 70.0 98.5 2.4 7.5 30.5 2.5 14.8 49.2 a/5/2005		
A/Vietnam/1194/2004 A/Vietnam/1194/2004 A/Indonesia/5/2005 N = number of subjects n (%) = number (percer 95% CI = 95% confiden PRE =Pre-vaccination PI(D21) = Post vaccina PII(D42) = Post vaccina Primary Outcome/Effi strains at Day 0 and Da Antibodies against	Group H5N1 Double H5N1 Double	Timing PRE PI(D21) PRE PI(D21) PII(D42) PRE PI(D21) PII(D42) PRE PI(D21) PII(D42) PRE PI(D21) PII(D42) S th titre within the s /er Limit, UL= Upp for H5N1 HI antib or persistence at D Timing	N 152 152 152 145 145 145 145 152 152 152 145 145 145 145 145 145 0 dies agai vay 180) 3	n 28 93 127 23 90 139 0 5 35 0 13 59 nge	% 18.4 61.2 83.6 15.9 62.1 95.9 0.0 3.3 23.0 0.0 9.0 40.7	SPR LL 12.6 53.0 76.7 10.3 53.6 91.2 0.0 1.1 16.6 0.0 4.9 32.6 04 and A/lr	95% C	UL 25.5 69.0 89.1 22.8 70.0 98.5 2.4 7.5 30.5 2.5 14.8 49.2		
A/Vietnam/1194/2004 A/Vietnam/1194/2004 A/Indonesia/5/2005 N = number of subjects n (%) = number (percer 95% CI = 95% confiden PRE =Pre-vaccination PI(D21) = Post vaccina PII(D42) = Post vaccina Primary Outcome/Effi strains at Day 0 and Da Antibodies against	Group H5N1 Double H5N1 Double	Timing PRE PI(D21) PRE PI(D21) PII(D42) PRE PI(D21) PII(D42) PRE PI(D21) PII(D42) PRE PI(D21) PII(D42) Sth titre within the s ver Limit, UL= Upp C for H5N1 HI antib presistence at D Timing	N 152 152 152 145 145 145 145 152 152 152 145 145 145 145 145 145 145 0 dies agai ay 180) 3	n 28 93 127 23 90 139 0 5 35 0 5 35 0 13 59 nge	% 18.4 61.2 83.6 15.9 62.1 95.9 0.0 3.3 23.0 0.0 9.0 40.7	SPR LL 12.6 53.0 76.7 10.3 53.6 91.2 0.0 1.1 16.6 0.0 4.9 32.6 04 and A/lr SPR %	95% C	UL 25.5 69.0 89.1 22.8 70.0 98.5 2.4 7.5 30.5 2.5 14.8 49.2 a/5/2005 % CI		
A/Vietnam/1194/2004 A/Indonesia/5/2005 N = number of subjects n (%) = number (percer 95% CI = 95% confiden PRE =Pre-vaccination PI(D21) = Post vaccina PII(D42) = Post vaccina Primary Outcome/Effi strains at Day 0 and Da Antibodies against	Group H5N1 Double H5N1 Double H5N1 Double H5N1 Double H5N1 intage) of subjects wi ince interval, LL= Low at Day 0 tion at Day 21 tion at Day 22 cacy Variable: SPR y 180 (ATP cohort fite Group	PRE PI(D21) PII(D42) St th titre within the s ver Limit, UL= Upp C for H5N1 HI antib presistence at D Timing	N 152 152 152 145 145 145 145 152 152 152 145 145 145 145 145 0 dies agai ay 180) 3	n 28 93 127 23 90 139 0 55 35 0 13 59 nge	% 18.4 61.2 83.6 15.9 62.1 95.9 0.0 3.3 23.0 0.0 9.0 40.7	SPR LL 12.6 53.0 76.7 10.3 53.6 91.2 0.0 1.1 16.6 0.0 4.9 32.6 04 and A/lr SPR %	95% C	CI UL 25.5 69.0 89.1 22.8 70.0 98.5 2.4 7.5 30.5 2.5 14.8 49.2 a/5/2005 % CI UL 20.0		

		•								
		Р	II(D180)	14	40	74	52.9	44.2	61.3
	Daubla HENI		PRE		13	35	21	15.6	9.9	22.8
		Р	II(D180)	13	31	91	69.5	60.8	77.2
			PRE	/	14	12	0	0.0	0.0	2.6
	H5N1	Р	II(D180)	14	40	5	3.6	1.2	8.1
A/Indonesia/5/2005			PRF	/	1:	35	0	0.0	0.0	27
	Double H5N1	P)	11	30	8	6.0	2.7	11 7
N = Number of subjects y	vith available resu	lts		/			0	0.1	2.1	11.7
n/0 – Number/percenter	o of coronrotoctor	l cubioata /l	JI titro	<u> </u>	1					
05% CL = 05% confidence		u subjects (i wor Limit L	II uu ∈ ₂ II – I lo	≤ 1.40 norli) mit					
95% CI = 95% connuence	E IIIEIVAI, LL – LU	wer Linnit, C	л – Ор	рег сі	IIII					
PIL(D180) - Post vaccing	tion at Day 180									
Primary Outcome/Efficient	Norichieles SDE	for UENI1	U ontib	odioo	oggingt	∧ /\/ioto	om/110	1/2004 on	d A/Indono	aia/5/2005
etraina at Day 0 and Man	th 12 (ATD schort		n anuu	Month	ayamsi (12)	Avvieuri	am/1194	4/2004 an		518/5/2005
Antibadian analinat			ince at	WOTU	112)				000	
Antibodies against	Group	IIM	ing	N			0/	SPR 0	F 0/ O 1	
							n	%	9	5% CI
			_						LL	
A/Vietnam/1194/2004	H5N1	PRE			1	12	22	19.6	12.7	28.2
		PII(M12)		1	12	49	43.8	34.4	53.4
	Double H5N	1 PRE	-		1	05	19	18.1	11.3	26.8
		PII(M12)		1	06	45	42.5	32.9	52.4
A/Indonesia/5/2005	H5N1	PRE	=		1	12	0	0.0	0.0	3.2
		PII(M12)		1	12	17	15.2	9.1	23.2
	Double H5N	1 PRE	<u> </u>		1	05	0	0.0	0.0	3.5
		PII(M12)		1	06	22	20.8	13.5	29.7
N = Number of subjects y	vith available resu	lts	/							-
95% CI = 95% confidence PRE = Pre-vaccination a PII(M12) = Post-vaccination Primary Outcome/Effica	e interval, LL = Lo : Day 0 ion at Month 12 cy Variable: SPR	ver Limit, L	JL = Up	per Li	mit res agai	inst A/Vi	ietnam/1	194/2004	and	
A/Indonesia/05/2005 stra		TP conort f	or persi	stence	e at ivior	1th 24)			000	
Antibodies against	Group		Timing	9		N _		0/	SPR 050	
							n	%	95%	
									LL	UL
A/Vietnam/1194/2004	H5N1		PII(M2	4)	8	86	32	37.2	27.0	48.3
	Double H5	N1	PII(M2	4)	8	81	25	30.9	21.1	42.1
A/Indonesia/5/2005	H5N1		PII(M2	4)	8	86	4	4.7	1.3	11.5
	Double H5	N1	PII(M2	4)	8	81	5	6.2	2.0	13.8
N = Number of subjects v n (%) = number (percenta 95% CI = 95% confidence PRE = Pre-vaccination at PII(M12)= Post-vaccinatio PII(M24)= Post-vaccinatio	vith available resul age) of seroprotect a interval, LL = Lov Day 0 on 2 at Month 12 on 2 at Month 24	ts ted subjects wer Limit, U	s (HI titr L = Upj	e ≥ 1: per Lir	40) nit					
Primary Outcome/Effica	cy Variable: Sero	positivity rat	es and	GMTs	s of neu	tralising	antibod	y titres ag	ainst	
A/Vietnam/1194/2004 and	A/Indonesia/5/20	05 strains a	t Days (0 and	42 – for	subset	of elder	ly subjects	s (ATP coh	ort for
immunogenicity)										
Antibodies against	Group	Timing	Ν		≥	1:28			GMT	
-				n	%	95%	6 CI	value	95	% CI
						LL	UL		LL	UL
A/Vietnam/1194/2004	H5N1	PRE	87	81	93.1	85.6	97.4	121.1	94.6	154.9
	-	PII(D42)	87	87	100	95.8	100	447.3	359.3	557.0
	Daula LICNA		00	77	02.0	06.2	000	112.5	00.7	120 5
	Double How1	FRE	0/	11	93.9	00.0	90.0	1 1 2 . 1	90.7	139.5
	Double Hon1		82	82	93.9	95 6	100	595.8	90.7 487 7	727 R

A/Indonesia/5/2005	H5N1	PI	RE	87	57	65.5	54.6	75.4	44.2	36.0	54.1
		PI	I(D42)	87	82	94.3	87.1	98.1	107.5	88.9	130.0
	Double	H5N1 PI	RE (82	48	58.5	47.1	69.3	39.7	32.0	49.3
		PI	I(D42)	82	82	100	95.6	100	169.6	144.7	198.9
N = Number of subjects n (%) = number (percer 95% CI = 95% confider PRE = Pre-vaccination PII(D42) = Post-vaccina Primary Outcome/Effi A/Vietnam/1194/2004 a	s with availab ntage) of serc nce interval, L at Day 0 ation 2 at Day cacy Variabl and A/Indone	le results ppositive subj L = Lower Li / 42 le: Seropositi sia/5/2005 st	ects (neu mit, UL = vity rates rains at E	utralis Upp and Day 18	sing tit er Lin GMT: 80–fo	tre $\ge 1:28$ hit s of neut r subset	8) ralising a	antibody y subjec	titres aga	inst phort for p	ersistence
at Day 180)				.,				,			
Antibodies against	Group	Timing	Ν			≥1:	28			GMT	
	n % 95% Cl value							95	% CI		
							LL	UL		LL	UL
	H5N1	PRE	77	7	73	94.8	87.2	98.6	131.3	101.0	170.7
A/Vietnam/1194/200		PII(D180)	76	7	76	100	95.3	100	218.2	172.4	276.2
4	Double	PRE	76	7	72	94.7	87.1	98.5	113.2	91.1	140.5
	H5N1	PII(D180)	73	1	73	100	95.1	100	260.9	207.7	327.8
		PRE	77	2	19	63.6	51.9	74.3	43.2	34.6	53.9
A/Indonesia/5/2005		PII(D180)	76	7	72	94.7	87.1	98.5	97.8	82.0	116.5
A/IIIdonesia/5/2005	Double	PRE	76	2	12	55.3	43.4	66.7	37.6	30.0	47.2
	H5N1	PII(D180)	73	7	72	98.6	92.6	100	134.5	113.4	159.7
A/Indonesia/5/2005 and persistence at Month 1	d A/Vietnam/ 2)	1194/2004 st	rains at N	/onth	12 –1	for subse	et of elde	erly subje	ects (ATP	cohort for	-
Antibodies against	Group	Timing	N			2	<u>≥ 1: 28</u>			GM	l
					n	%	95%		val	ue <u>95%</u>	CI
					0-			UL			
A/Vietnam/1194/2004	H5N1	PRE	69		65	94.2	85.8	3 98	.4 134	1.0 101.	1 1//./
	Daubl		69		69 67	100	94.8	<u>s 10</u>	$\frac{1}{4}$ $\frac{274}{400}$	1.7 213.	4 353.5
		PKE	/1		0/ 74	94.4	86.2	2 98	.4 108		135.9
Alladones: -/5/2005			/1		1	100	94.9	10	268		4 341.8
A/Indonesia/3/2005		PRE DII/M40	60		40 59	05.2	52.0 70 /		.3 40. g 00	5 51.U	09.0 107.0
	Doublo		71		38	04. I	10.	2 65	.0 02. 5 26	0.00 0 0 0 0 0 0 0	107.9
	H5N1		71		50 65	01.5	41. 821		.J JU. 8 110	20.0	40.7
N = Number of subjects	with availab	le resulte			00	51.0	02.3	, 30	.0 118	.0 J 94.0	192.7
N/% = number/percent	ane of serond	ie results sitive subiec	ts (neutr	alisin	n titro	> 1.28)					
95% CI = $95%$ confider	nce interval. L	L = Lower Li	mit. UL =	: Upp	er Lin	- 1.20) nit					
PRE = Pre-vaccination	at Day 0	_0.701 El	, ७८	-44		•					
PII(M12) = Post-vaccin	ation vaccina	tion at Month	12								
Primary Outcome/Efficacy Variable: Seropositivity rates and GMTs of neutralising antibody titres against A/Vietnam/1194/2004 and A/Indonesia/05/2005 strains at Month 24 – for subset of elderly subjects (ATP cohort for persistence at Month 24)											
Antibodies	Group	Timina	N			≥1	:28			GMT	
against	r -	-0			n	%	9	5% CI	value	e 9	5% CI
-							LL	UL		LL	UL
A/Vietnem/4404/200	H5N1	PII(M24)	49	Δ	lg	100	927	/ 10() 391 () 295.5	517 5

4	Double	PII(M24)	54	54	100	93.4	100	382.8	317.4	461.6
Alladonosio/5/200			40	11	00.0	77.0	06.6	75 /	57.0	00.4
A/Indonesia/5/200		PII(IVI24)	49	44 52	09.0	11.0	90.0	75.4	57.Z	99.4
5	H5N1	P11(1V124)	54	52	90.3	07.3	99.5	04.9	07.0	107.0
GMT = Geometric Me	an antibody t	itre								
N = Number of subject	ts with availa	ble results	S			•				
n (%) = number (perc	entage) of sei	ropositive	subjects (ne	eutralising ti	tre \geq 1:2	8)				
PRF = Pre-vaccinatio	n at Day 0	LL - LOW		- Opper Lin	III					
PII(M12)= Post-vaccir	nation 2 at Mo	onth 12								
PII(M24)= Post-vaccir	nation 2 at Mo	onth 24								
Primary Outcome/Efficacy Variable: SCR for neutralising antibody response against A/Vietnam/1194/2004 and A/Indonesia/5/2005 strains at Day 42 – for subset of elderly subjects(ATP cohort for immunogenicity)										
Antibodies against	Group		Timing	N			S	SCR		
, i i i i i i i i i i i i i i i i i i i			Ŭ		n	%		95	% CI	
								LL	l	JL
A/Vietnam/1194/2004	H5N1		PII(D42)	87	39	44.8	3	34.1	5	5.9
	Double	H5N1	PII(D42)	82	46	56.1	4	14.7	6	7.0
A/Indonesia/5/2005	H5N1		PII(D42)	87	25	28.7	-	19.5	3	9.4
	Double	H5N1	PII(D42)	82	40	48.8	3	87.6	6	0.1
SCR defined as:										
For initially seronegative	/e subjects, a	ntibody tit	$re \ge 1:56 af$	ter vaccinat	on					
For initially seropositiv	e subjects, a	ntibody titi	re after vacc	cination ≥ 4	fold the	pre-vacc	cination an	tibody titre	•	
N = Number of subject	s with pre- ar	id post-va	ccination res	sults availat	le					
11(%) - 10110er (perce	ntage) of sere		u subjects r Limit III -	- Unner Lim	i+					
35 /0 CI - 35 /0 COIIIUE	nce interval, i		- Linit, OL -	- оррег спп	π.					
PII(D42) = Post-vaccir	nation 2 at Da	iv 42								
PII(D42) = Post-vaccii	nation 2 at Da	iy 42 Ie: SCR fo	or neutralisir	na antibody	respons	e agains	t A/Vietna	m/1194/20	04 and	
PII(D42) = Post-vaccin Primary Outcome/Eff A/Indonesia/5/2005 str	nation 2 at Da icacy Variab ains at Day 1	<u>iy 42</u> le: SCR fo 80 - for su	or neutralisir Ibset of elde	ng antibody erly subjects	respons (ATP co	e agains	t A/Vietna	m/1194/20 ce at Day 1	04 and 80)	
PII(D42) = Post-vaccin Primary Outcome/Eff A/Indonesia/5/2005 str Antibodies against	nation 2 at Da icacy Variab ains at Day 1 Grou	iy 42 le: SCR fo 80 - for su p	or neutralisir ibset of elde Timing	ng antibody erly subjects N	respons (ATP co	e agains bhort for	t A/Vietna persistenc	m/1194/20 e at Day 1	104 and 180)	
PII(D42) = Post-vaccin Primary Outcome/Eff A/Indonesia/5/2005 str Antibodies against	nation 2 at Da icacy Variab ains at Day 1 Grou	ny 42 le: SCR fo 80 - for su p	or neutralisir ibset of elde Timing	ng antibody erly subjects N	respons (ATP co n	e agains bhort for	t A/Vietna persistenc \$	m/1194/20 ee at Day 1 SCR	04 and 80) 95% CI	
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For initially seronegative subjects, antibody titre \geq 1:56 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

PII(M12) = Post-vaccination at Month 12

Primary Outcome/Efficacy Variable: SCR for neutralising antibody titres against A/Vietnam/1194/2004 and A/Indonesia/05/2005 strains at Month 24 – for subset of elderly subjects (ATP cohort for persistence at Month 24)

Antibodies against	Group	Timing	N	SCR			
				n	n % 95% C		CI
						LL	UL
A/Vietnam/1194/200	H5N1	PII(M24)	49	18	36.7	23.4	51.7
4	Double H5N1	PII(M24)	54	22	40.7	27.6	55.0
A/Indonesia/5/2005	H5N1	PII(M24)	49	6	12.2	4.6	24.8
	Double H5N1	PII(M24)	54	16	29.6	18.0	43.6

Seroconversion defined as:

For initially seronegative subjects, antibody titre \geq 1:56 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

PII(M12)= Post-vaccination 2 at Month 12

PII(M24)= Post-vaccination 2 at Month 24

Secondary Outcome/Efficacy Variables: Descriptive Statistics on the frequency cytokine-positive T-cells (per 10⁶) for CD4.CD40L, CD4.all doubles (T-cells producing at least 2 cytokines), CD4.IL-2, CD4.TNFα, CD4.INFγ stimulated by H5N1 A/Vietnam/1194/2004 strain (ATP cohort for immunogenicity)

Test description	Group	Timing	N	GM	Mean	SD
		PRE	129	393.71	620.14	590.66
	H5N1	PI(D21)	112	1407.29	1845.30	1354.44
CD4 all daubles		PII(D42)	120	2260.19	3034.88	2242.14
CD4. all doubles	Double	PRE	122	495.77	670.50	606.84
		PI(D21)	110	1793.92	2315.24	1867.92
	TIONT	PII(D42)	118	3049.03	4171.24	4208.17
		PRE	129	388.69	604.88	571.91
	H5N1	PI(D21)	112	1374.26	1782.67	1304.02
		PII(D42)	120	2198.66	2943.00	2165.46
CD4.CD40L	Doublo	PRE	122	485.71	655.20	594.88
		PI(D21)	110	1731.58	2247.71	1828.74
		PII(D42)	118	2971.34	4056.64	4076.52
	H5N1	PRE	129	376.03	571.24	545.75
		PI(D21)	112	1318.03	1716.82	1250.79
		PII(D42)	120	2086.84	2813.43	2086.66
CD4.1L-2	Daubla	PRE	122	461.23	609.22	552.91
		PI(D21)	110	1651.88	2146.25	1776.72
	TIJINT	PII(D42)	118	2762.65	3778.94	3720.42
		PRE	129	270.99	459.03	500.13
	H5N1	PI(D21)	112	685.44	1026.93	884.75
		PII(D42)	120	1123.16	1626.48	1356.18
CD4.INFY	Double	PRE	122	343.35	505.50	549.24
		PI(D21)	110	997.15	1291.85	1023.96
	TIONT	PII(D42)	118	1535.37	2293.17	2864.48
		PRE	129	310.91	464.85	486.27
CD4.TNFa	H5N1	PI(D21)	112	932.64	1239.38	974.72
		PII(D42)	120	1595.64	2227.27	1798.95

Daubla	PRE	122	358.27	518.70	538.07
	PI(D21)	110	1207.95	1641.36	1527.86
TIONT	PII(D42)	118	2170.46	3100.96	3380.48

PRE = Pre-vaccination

PI(D21) = Post vaccination at Day 21

PII(D42) = Post vaccination at Day 42

All doubles: T-cells producing at least 2 cytokines

CD4-CD40L: CD4 T-cells producing at least CD40L and another cytokine

CD4-IL-2: CD4 T-cells producing at least IL2 and another cytokine

CD4-INF_Y: CD4 T-cells producing at least INF gamma and another cytokine

CD4-TNF α : CD4 T-cells producing at least TNF alpha and another cytokine

N = number of subjects with available results

GM= Geometric Mean

SD = Standard Deviation

Secondary Outcome/Efficacy Variables: Descriptive Statistics on the frequency cytokine-positive T-cells (per million T-cells) for CD4.CD40L, CD4.all doubles, CD4.IL-2, CD4.TNFα, CD4.INFγ stimulated by H5N1 A/Vietnam/1194/2004 strain at Day 180 (ATP cohort for persistence at Day 180)

Test description	Group	Timing	N	GM	Mean	SD
		PRE	120	386.36	626.66	609.62
CD4 all daubles		PII(D180)	132	1247.34	1521.60	1000.47
CD4. all doubles	Double HEN1	PRE	114	478.17	642.69	580.86
		PII(D180)	122	1515.07	1985.20	1982.71
		PRE	120	382.75	611.22	588.69
		PII(D180)	132	1188.86	1449.26	939.31
CD4.CD40L	Double HEN1	PRE	114	468.50	627.99	570.09
		PII(D180)	122	1455.68	1886.15	1789.27
		PRE	120	369.09	577.90	563.25
		PII(D180)	132	1172.16	1434.47	957.55
604.IL-2	Double HEN1	PRE	114	441.56	582.12	538.27
		PII(D180)	122	1433.08	1887.17	1921.82
		PRE	120	264.43	461.18	514.57
		PII(D180)	132	654.11	850.89	661.08
CD4.INF-γ	Double HEN1	PRE	114	325.98	476.00	531.62
		PII(D180)	122	763.06	1078.66	1243.60
		PRE	120	310.14	472.11	498.36
		PII(D180)	132	937.82	1182.06	839.91
CD4.1NF- α	Daubla HEN1	PRE	114	342.26	496.33	530.44
		PII(D180)	122	1143.69	1525.03	1444.11

PRE = Pre-vaccination at Day 0

PII(D180) = Post-vaccination at Day 180

All doubles: T-cells producing at least 2 cytokines

CD4-CD40L: CD4 T-cells producing at least CD40L and another cytokine

CD4-IL-2: CD4 T-cells producing at least IL2 and another cytokine

CD4-INF7: CD4 T-cells producing at least INF gamma and another cytokine

CD4-TNFa: CD4 T-cells producing at least TNF alpha and another cytokine

N = number of subjects with available results

GM = Geometric Mean

SD = Standard Deviation

Secondary Outcome/Efficacy Variables: Descriptive Statistics on the frequency cytokine-positive T-cells (per million T-cells) for CD4.CD40L, CD4.all doubles, CD4.IL-2, CD4.TNFα, CD4.INFγ stimulated by H5N1 A/Vietnam/1194/2004 strain at Month 12 (ATP cohort for persistence at Month 12)

Test description	Group	Timing	N	GM	Mean	SD
CD4. all doubles	H5N1	PRE	96	367.90	610.44	640.49
		PII(M12)	90	898.52	1270.86	1050.39
	Double H5N1	PRE	89	476.14	619.53	414.17

		PII(M12)	91	1170.36	1480.40	1021.43
CD4.CD40L	H5N1	PRE	96	364.80	595.16	620.28
		PII(M12)	90	934.35	1252.94	1020.83
	Double H5N1	PRE	89	463.00	606.72	411.14
		PII(M12)	91	1146.47	1453.32	1002.22
CD4.IL-2	H5N1	PRE	96	355.29	566.08	595.83
		PII(M12)	90	902.69	1217.27	1006.77
	Double H5N1	PRE	89	453.83	562.74	380.64
		PII(M12)	91	1118.63	1405.66	973.32
CD4.INF-γ	H5N1	PRE	96	242.71	456.28	553.41
•		PII(M12)	90	442.66	703.12	743.99
	Double H5N1	PRE	89	321.28	453.17	348.03
		PII(M12)	91	586.60	772.51	577.71
CD4.TNF- α	H5N1	PRE	96	307.62	473.28	536.35
		PII(M12)	90	678.60	993.50	870.28
	Double H5N1	PRE	89	345.91	478.76	355.38
		PII(M12)	91	884.64	1155.80	847.51

PRE = Pre-vaccination at Day 0

PII(M12) = Post-vaccination at Month 12

All doubles: T-cells producing at least 2 cytokines

CD4-CD40L: CD4 T-cells producing at least CD40L and another cytokine

CD4-IL-2: CD4 T-cells producing at least IL2 and another cytokine

CD4-INF_Y: CD4 T-cells producing at least INF gamma and another cytokine

CD4-TNFa: CD4 T-cells producing at least TNF alpha and another cytokine

N = number of subjects with available results

GM = Geometric Mean

SD = Standard Deviation

Secondary Outcome/Efficacy Variables: Descriptive Statistics on the frequency cytokine-positive CD4 T-cells at Month 24 (per 10⁶) for CD4.CD40L, CD4.all doubles, CD4.IL-2, CD4.TNFα, CD4.INFγ stimulated by H5N1 A/Vietnam/1194/2004 strain (ATP cohort for persistence at Month 24)

Test description	Group	Timing	N	GM	Mean	SD
CD4 all doubles	H5N1	PII(M24)	73	779.93	1052.59	771.46
	Double H5N1	PII(M24)	72	1126.86	1483.86	1375.31
CD4-CD40L	H5N1	PII(M24)	73	710.53	1002.15	712.25
	Double H5N1	PII(M24)	72	1041.16	1399.31	1356.01
CD4-IL-2	H5N1	PII(M24)	73	769.56	1009.84	718.28
	Double H5N1	PII(M24)	72	1043.95	1400.18	1333.41
CD4-INF-γ	H5N1	PII(M24)	73	455.05	675.34	608.16
•	Double H5N1	PII(M24)	72	651.02	932.38	947.13
CD4-TNF-a	H5N1	PII(M24)	73	500.82	734.85	555.63
	Double H5N1	PII(M24)	72	806.94	1096.81	1012.40

CD4 All doubles:CD4 T-cells producing at least 2 cytokines

CD4-CD40L: CD4 T-cells producing at least CD40L and another cytokine

CD4-IL-2: CD4 T-cells producing at least IL2 and another cytokine

CD4-INF_Y: CD4 T-cells producing at least INF gamma and another cytokine

CD4-TNFa: CD4 T-cells producing at least TNF alpha and another cytokine

N = number of subjects with available results

GM= Geometric Mean

SD = Standard Deviation

PII(M24) = Post-vaccination 2 at Month 24

Secondary Outcome/Efficacy Variables: Descriptive Statistics on the frequency cytokine-positive T-cells (per 10 ⁶) for									
CD8.all doubles, CD8.CD40L, CD8.IL-2, CD8.TNFα, CD8.INFγ stimulated by H5N1 A/Vietnam/1194/2004 strain (ATP									
cohort for immunogenicity)									
Test description	Group	Timina	N	GM	Maan	en.			

Test description	Group	Timing	Ν	GM	Mean	SD
CD8.all doubles	H5N1	PRE	129	83.30	299.57	407.94

		PI(D21)	111	70.23	297.30	391.63
		PII(D42)	120	77.73	296.52	499.25
	Daubla	PRE	121	71.93	352.07	626.44
		PI(D21)	109	77.70	312.37	661.43
		PII(D42)	118	79.56	370.58	765.47
		PRE	129	3.37	24.04	52.35
	H5N1	PI(D21)	111	3.90	26.86	52.29
		PII(D42)	120	5.32	34.11	100.78
CD0.CD40L	Daubla	PRE	121	3.58	20.88	48.88
		PI(D21)	109	5.61	24.78	34.07
		PII(D42)	118	5.23	30.97	51.86
		PRE	129	53.90	190.62	241.03
	H5N1	PI(D21)	111	45.48	197.19	251.49
		PII(D42)	120	42.77	181.76	261.13
CD0.IL-2	Daubla	PRE	121	59.70	218.11	340.60
		PI(D21)	109	45.97	200.17	342.71
		PII(D42)	118	50.37	228.35	413.85
		PRE	129	83.14	287.51	394.32
	H5N1	PI(D21)	111	61.44	289.99	390.60
		PII(D42)	120	55.71	280.14	506.29
CDO.INFY	Daubla	PRE	121	80.54	339.86	618.55
		PI(D21)	109	55.07	290.79	661.84
	TIONT	PII(D42)	118	63.71	353.79	767.88
		PRE	129	63.19	239.59	355.75
	H5N1	PI(D21)	111	55.42	225.67	306.06
		PII(D42)	120	59.51	239.68	434.37
CD0.INFα	Daubla	PRE	121	45.34	294.21	573.91
		PI(D21)	109	63.94	261.77	609.54
		PII(D42)	118	59.10	315.86	689.32

PRE = Pre-vaccination

PI(D21) = Post vaccination at Day 21

PII(D42) = Post vaccination at Day 42

All doubles: T-cells producing at least 2 cytokines

CD8-CD40L: CD8 T-cells producing at least CD40L and another cytokine

CD8-IL-2: CD8 T-cells producing at least IL2 and another cytokine

CD8-INF_Y: CD8 T-cells producing at least INF gamma and another cytokine

CD8-TNF α : CD8 T-cells producing at least TNF alpha and another cytokine

N = number of subjects with available results

GM= Geometric Mean

SD = Standard Deviation

Secondary Outcome/Efficacy Variables: Descriptive Statistics on the frequency cytokine-positive T-cells (per million T-cells) for CD8.all doubles, CD8.CD40L, CD8.IL-2, CD8.TNF-α, CD8.INF-γ stimulated by H5N1 A/Vietnam/1194/2004 strain at Day 180 (ATP cohort for persistence at Day 180)

Test description	Group	Timing	N	GM	Mean	SD
		PRE	120	77.34	275.28	332.50
	ואונח	PII(D180)	132	32.11	185.05	293.81
CD0.all doubles	Double H5N1	PRE	PRE 113 69.86	69.86	360.58	644.26
		PII(D180)	121	41.28	282.34	753.94
		PRE	120	3.21	20.57	44.56
	ואונח	PII(D180)	132	2.04	11.54	26.32
CD0.CD40L	Double H5N1	PRE	113	3.60	22.23	51.42
	Double LIDINT	PII(D180)	121	2.47	57.69	499.31
CD8.IL-2		PRE	120	51.91	177.63	201.96
		PII(D180)	132	18.78	113.14	178.46

	Double HEN1	PRE	113	58.85	222.50	349.86
		PII(D180)	121	23.70	200.64	704.78
		PRE	120	80.00	264.55	321.00
		PII(D180)	132	26.37	171.13	288.43
CDO.INFY	Double UEN1	PRE	113	82.46	352.20	635.24
		PII(D180)	121	41.21	257.12	663.40
		PRE	120	61.36	222.37	286.67
	TIJNT	PII(D180)	132	22.30	157.54	270.88
CD8.TNFa	Double H5N1	PRE	113	46.58	303.72	590.59
		PII(D180)	121	36.68	212.20	390.84

PRE = Pre-vaccination at Day 0

PII(D180) = Post-vaccination at Day 180

All doubles: T-cells producing at least 2 cytokines

CD8-CD40L: CD8 T-cells producing at least CD40L and another cytokine

CD8-IL-2: CD8 T-cells producing at least IL2 and another cytokine

CD8-INF_Y: CD8 T-cells producing at least INF gamma and another cytokine

CD8-TNF a: CD8 T-cells producing at least TNF alpha and another cytokine

N = number of subjects with available results

GM= Geometric Mean

SD = Standard Deviation

Secondary Outcome/Efficacy Variables: Descriptive Statistics on the frequency cytokine-positive T-cells (per million T-cells) for CD8.all doubles, CD8.CD40L, CD8.IL-2, CD8.TNF- α , CD8.INF- γ stimulated by H5N1 A/Vietnam/1194/2004 strain at Month 12 (ATP cohort for persistence at Month 12)

Test description	Group	Timing	N	GM	Mean	SD
CD8.all doubles	H5N1	PRE	96	76.10	259.68	284.24
		PII(M12)	90	34.28	175.46	275.22
	Double H5N1	PRE	88	64.77	350.23	653.58
		PII(M12)	91	27.88	167.02	261.68
CD8.CD40L	H5N1	PRE	96	2.78	15.96	30.19
		PII(M12)	90	2.08	11.93	28.46
	Double H5N1	PRE	88	3.21	18.03	33.42
		PII(M12)	91	2.99	15.43	28.90
CD8.IL-2	H5N1	PRE	96	48.96	175.27	194.43
		PII(M12)	90	18.84	112.71	167.58
	Double H5N1	PRE	88	60.23	207.74	307.82
		PII(M12)	91	19.95	108.04	164.36
CD8.INFγ	H5N1	PRE	96	76.43	250.39	281.06
		PII(M12)	90	29.13	155.96	271.12
	Double H5N1	PRE	88	76.94	343.09	649.61
		PII(M12)	91	20.75	151.33	260.19
CD8.TNF α	H5N1	PRE	96	55.98	206.97	232.89
		PII(M12)	90	35.67	159.66	251.66
	Double H5N1	PRE	88	41.97	293.76	597.80
		PII(M12)	91	28.15	154.10	246.49

PRE = Pre-vaccination at Day 0

PII(M12) = Post-vaccination at Month 12

All doubles: T-cells producing at least 2 cytokines

CD8-CD40L: CD8 T-cells producing at least CD40L and another cytokine

CD8-IL-2: CD8 T-cells producing at least IL2 and another cytokine

CD8-INF_Y: CD8 T-cells producing at least INF gamma and another cytokine

CD8-TNF a: CD8 T-cells producing at least TNF alpha and another cytokine

N = number of subjects with available results

GM= Geometric Mean

SD = Standard Deviation

Secondary Outcome/Efficacy Variables: Descriptive Statistics on the frequency cytokine-positive CD8 T-cells (per 106) at

Month 24 CD8.all doubles (T-cells producing at least 2 cytokines), CD8.CD40L, CD8.IL-2, CD8.TNF α , CD8.INF γ stimulated by H5N1 A/Vietnam/1194/2004 strain (ATP cohort for persistence at Month 24)

Test description	Group	Timing	N	GM	Mean	SD
CD8 all doubles	H5N1	PII(M24)	73	8.05	57.37	94.19
	Double H5N1	PII(M24)	72	21.67	153.63	258.83
CD8-CD40L	H5N1	PII(M24)	73	1.94	11.99	29.28
	Double H5N1	PII(M24)	72	2.58	14.43	32.70
CD8-IL-2	H5N1	PII(M24)	73	5.04	37.90	65.04
	Double H5N1	PII(M24)	72	8.16	84.83	181.28
CD8-INF-γ	H5N1	PII(M24)	73	7.43	55.49	93.13
·	Double H5N1	PII(M24)	72	23.39	153.01	257.70
CD8-TNF-α	H5N1	PII(M24)	73	4.76	35.49	65.03
	Double H5N1	PII(M24)	72	17.22	131.89	231 77

CD8-All doubles: CD8-T-cells producing at least 2 cytokines

CD8-CD40L: CD8 T-cells producing at least CD40L and another cytokine

CD8-IL-2: CD8 T-cells producing at least IL2 and another cytokine

CD8-INF_Y: CD8 T-cells producing at least INF gamma and another cytokine

CD8-TNF α : CD8 T-cells producing at least TNF alpha and another cytokine

N = number of subjects with available results

GM= Geometric Mean

SD = Standard Deviation

PII(M24) = Post-vaccination 2 at Month 24

Secondary Outcome/Efficacy Variables: Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total Vaccinated cohort)

			H51	V1 Group			Double H5N1 Group					
Symptom	Intensity	Ν	n	%	95%	% CI	Ν	n	%	95	6% CI	
					LL	UL				LL	UL	
	Dose 1											
Ecchymosis	Any	164	1	0.6	0.0	3.4	159	5	3.1	1.0	7.2	
	> 100 mm	164	0	0.0	0.0	2.2	159	0	0.0	0.0	2.3	
Induration	Any	164	7	4.3	1.7	8.6	159	6	3.8	1.4	8.0	
	> 100 mm	164	0	0.0	0.0	2.2	159	0	0.0	0.0	2.3	
Pain	Any	164	56	34.1	26.9	41.9	159	63	39.6	32.0	47.7	
	Grade 3	164	0	0.0	0.0	2.2	159	0	0.0	0.0	2.3	
Redness	Any	164	9	5.5	2.5	10.2	159	19	11.9	7.4	18.0	
	> 100 mm	164	0	0.0	0.0	2.2	159	1	0.6	0.0	3.5	
Swelling	Any	164	9	5.5	2.5	10.2	159	8	5.0	2.2	9.7	
	> 100 mm	164	0	0.0	0.0	2.2	154	0	0.0	0.0	2.3	
				Dos	e 2							
Ecchymosis	Any	161	0	0.0	0.0	2.3	154	0	0.0	0.0	2.4	
	> 100 mm	161	0	0.0	0.0	2.3	154	0	0.0	0.0	2.4	
Induration	Any	161	4	2.5	0.7	6.2	154	11	7.1	3.6	12.4	
	> 100 mm	161	0	0.0	0.0	2.3	154	0	0.0	0.0	2.4	
Pain	Any	161	50	31.1	24.0	38.8	154	57	37.0	29.4	45.2	
	Grade 3	161	0	0.0	0.0	2.3	154	2	1.3	0.2	4.6	
Redness	Any	161	12	7.5	3.9	12.7	154	20	13.0	8.1	19.3	
	> 100 mm	161	0	0.0	0.0	2.3	154	0	0.0	0.0	2.4	
Swelling	Any	161	14	8.7	4.8	14.2	154	10	6.5	3.2	11.6	
	> 100 mm	161	0	0.0	0.0	2.3	313	0	0.0	0.0	2.4	
				Across	doses							
Ecchymosis	Any	164	1	0.6	0.0	3.4	159	5	3.1	1.0	7.2	
	> 100 mm	164	0	0.0	0.0	2.2	159	0	0.0	0.0	2.3	
Induration	Any	164	10	6.1	3.0	10.9	159	15	9.4	5.4	15.1	

	> 100 mm	164	0	0.0) 0.0	0 2	2	159	0	0	.0 0	.0	2.3
Pain	Any	164	69	42.	1 34.	.4 50	.0	159	75	5 47	'.2 <u>3</u>	9.2	55.2
	Grade 3	164	0	0.0) 0.0	0 2	2	159	2	1	.3 (.2	4.5
Redness	Any	164	19	11.	6 7.	1 17	.5	159	30) 18	3.9 1	3.1	25.8
	> 100 mm	164	0	0.0) 0.0	0 2	2	159	1	0	.6 (.0	3.5
Swelling	Any	164	19	11.	6 7.	1 17	.5	159	15	5 9	.4 5	.4	15.1
U U	> 100 mm	164	0	0.0) 0.0	0 2	2	159	0	0	.0 0	.0	2.3
Any = occurrence	of any solicited	local sy	mptom	regardles	ss of thei	ir intens	ity g	grade	I		I		
Grade 3 pain = pa	in that prevente	d norm	al activit	y			, ,						
N= number of sub	jects with at lea	st one c	locume	nted dose	;								
n (%) = number (p	ercentage) of s	ubjects	reportin	g at least	once th	e symp	tom						
95% CI = 95% cor	nfidence interva	I, LL = L	ower L	mit, UL =	Upper L	imit							
Secondary Outco	ome/Efficacy V	ariable	s: Incide	ence of so	plicited g	eneral	symj	ptoms	reported	d during	the 7-d	ay (Days	0-6)
post-vaccination p	eriod following	each do	se and	overall (1	otal Vac	cinated	coh	nort)			<u> </u>		
				H5	N1 Grou	ıp				D	ouble H	5N1	
Cummtom	Interester	1	N		0/	0	E0/ /	0	N		0/	0.50	
Symptom	Polationsh	in	N	n	%	9	5%		N	n	%	95	
	Relationsh	ιμ			Doco 1	LL		UL					UL
Arthralaia	Δηγ		16/	5	20	10		70	150	7	11	1.8	80
Artinaigia	Grade 3		16/	0	0.0	0.0		2.2	159	2	1 3	0.2	1.5
-	Related		16/	0	0.0	0.0		2.2	150	1	0.6	0.2	3.5
Fatique	Δην		164	16	9.8	5.7		15.4	159	26	16.4	11.0	23.0
1 aligue	Grade 3		164	10	0.6	0.0		34	159	20	13	0.2	4 5
-	Related		164	1	0.0	0.0		3.4	159	4	2.5	0.2	6.3
Fever/	>37.5		164	0	0.0	0.0		22	159	2	1.3	0.7	4.5
(Axillary) (°C)	>39.0		164	0	0.0	0.0		2.2	159	1	0.6	0.0	3.5
(Related		164	0	0.0	0.0		22	159	0	0.0	0.0	2.3
Headache	Anv		164	15	9.1	5.2		14.6	159	18	11.3	6.8	17.3
	Grade 3		164	0	0.0	0.0		2.2	159	0	0.0	0.0	2.3
	Related		164	0	0.0	0.0		2.2	159	4	2.5	0.7	6.3
Myalgia	Any		164	13	7.9	4.3		13.2	159	23	14.5	9.4	20.9
	Grade 3		164	0	0.0	0.0		2.2	159	3	1.9	0.4	5.4
	Related		164	0	0.0	0.0		2.2	159	3	1.9	0.4	5.4
Shivering	Any		164	0	0.0	0.0		2.2	159	3	1.9	0.4	5.4
	Grade 3		164	0	0.0	0.0		2.2	159	1	0.6	0.0	3.5
	Related		164	0	0.0	0.0		2.2	159	1	0.6	0.0	3.5
Sweating	Any		164	8	4.9	2.1		9.4	159	11	6.9	3.5	12.0
	Grade 3		164	0	0.0	0.0		2.2	159	1	0.6	0.0	3.5
	Related		164	0	0.0	0.0		2.2	159	0	0.0	0.0	2.3
					Dose 2						_	_	_
Arthralgia	Any		161	10	6.2	3.0		11.1	154	9	5.8	2.7	10.8
	Grade 3	3	161	1	0.6	0.0		3.4	154	0	0.0	0.0	2.4
	Related	1	161	0	0.0	0.0		2.3	154	2	1.3	0.2	4.6
Fatigue	Any		161	26	16.1	10.8	}	22.8	154	28	18.2	12.4	25.2
	Grade 3	3	161	1	0.6	0.0		3.4	154	4	2.6	0.7	6.5
	Related	1	161	0	0.0	0.0		2.3	154	5	3.2	1.1	7.4
Fever/ (Axillary)	>37.5		161	2	1.2	0.2		4.4	154	3	1.9	0.4	5.6
(°C)	>39.0		161	1	0.6	0.0		3.4	154	0	0.0	0.0	2.4
	Related	1	161	0	0.0	0.0		2.3	154	1	0.6	0.0	3.6
Headache	Any		161	20	12.4	7.8		18.5	154	27	17.5	11.9	24.5
	Grade 3	3	161	0	0.0	0.0		2.3	154	1	0.6	0.0	3.6
	Related	1	161	2	1.2	0.2		4.4	154	4	2.6	0.7	6.5
Myalgia	Any		161	15	9.3	5.3		14.9	154	13	8.4	4.6	14.0

	Grade 3	161	1	0.6	0.0	3.4	154	1	0.6	0.0	3.6
	Related	161	2	1.2	0.2	4.4	154	2	1.3	0.2	4.6
Shivering	Any	161	2	1.2	0.2	4.4	154	7	4.5	1.8	9.1
_	Grade 3	161	1	0.6	0.0	3.4	154	0	0.0	0.0	2.4
	Related	161	0	0.0	0.0	2.3	154	2	1.3	0.2	4.6
Sweating	Any	161	12	7.5	3.9	12.7	154	12	7.8	4.1	13.2
	Grade 3	161	0	0.0	0.0	2.3	154	0	0.0	0.0	2.4
	Related	161	0	0.0	0.0	2.3	154	1	0.6	0.0	3.6
			Acr	oss dose	s						
Arthralgia	Any	164	13	7.9	4.3	13.2	159	13	8.2	4.4	13.6
_	Grade 3	164	1	0.6	0.0	3.4	159	2	1.3	0.2	4.5
	Related	164	0	0.0	0.0	2.2	159	2	1.3	0.2	4.5
Fatigue	Any	164	32	19.5	13.7	26.4	159	39	24.5	18.1	32.0
_	Grade 3	164	2	1.2	0.1	4.3	159	6	3.8	1.4	8.0
	Related	164	1	0.6	0.0	3.4	159	8	5.0	2.2	9.7
Fever/ (Axillary)	>37.5	164	2	1.2	0.1	4.3	159	5	3.1	1.0	7.2
(°C)	>39.0	164	1	0.6	0.0	3.4	159	1	0.6	0.0	3.5
	Related	164	0	0.0	0.0	2.2	159	1	0.6	0.0	3.5
Headache	Any	164	27	16.5	11.1	23.0	159	34	21.4	15.3	28.6
	Grade 3	164	0	0.0	0.0	2.2	159	1	0.6	0.0	3.5
	Related	164	2	1.2	0.1	4.3	159	6	3.8	1.4	8.0
Myalgia	Any	164	24	14.6	9.6	21.0	159	28	17.6	12.0	24.4
	Grade 3	164	1	0.6	0.0	3.4	159	4	2.5	0.7	6.3
	Related	164	2	1.2	0.1	4.3	159	4	2.5	0.7	6.3
Shivering	Any	164	2	1.2	0.1	4.3	159	9	5.7	2.6	10.5
	Grade 3	164	1	0.6	0.0	3.4	159	1	0.6	0.0	3.5
	Related	164	0	0.0	0.0	2.2	159	2	1.3	0.2	4.5
Sweating	Any	164	16	9.8	5.7	15.4	159	19	11.9	7.4	18.0
_	Grade 3	164	0	0.0	0.0	2.2	159	1	0.6	0.0	3.5
	Related	164	0	0.0	0.0	2.2	159	1	0.6	0.0	3.5

Any: occurrence of any solicited general symptom regardless of their intensity grade or relationship to vaccination Grade 3 arthralgia, fatigue, headache, myalgia, shivering, sweating: symptom that prevented normal activity Related = general symptom assessed by the investigator as causally related to the study vaccination

N= number of subjects with at least one 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/Efficacy Variables: Haematological and biochemical levels with respect to normal ranges (Total Vaccinated cohort)

Laboratory	Timing	H5N1 Group							Double H5N1						
parameter	_		Be	low	Wi	ithin	Α	bove		Be	elow	Wi	thin	A	oove
		N	n	%	n	%	n	%	N	n	%	n	%	n	%
Alanine	PRE	165	0	0.00	152	92.12	13	7.88	159	1	0.63	152	95.60	6	3.77
Aminotransferase	PI(Day 2)	165	0	0.00	152	92.12	13	7.88	158	1	0.63	151	95.57	6	3.80
	PI(Day 21)	163	0	0.00	153	93.87	10	6.13	156	1	0.64	144	92.31	11	7.05
	PII(Day 23)	163	0	0.00	152	93.25	11	6.75	155	1	0.65	146	94.19	8	5.16
Aspartate	PRE	165	0	0.00	154	93.33	11	6.67	159	0	0.00	150	94.34	9	5.66
Aminotransferase	PI(Day 2)	165	0	0.00	154	93.33	11	6.67	158	0	0.00	152	96.20	6	3.80
	PI(Day 21)	163	0	0.00	154	94.48	9	5.52	156	0	0.00	146	93.59	10	6.41
	PII(Day 23)	163	0	0.00	153	93.87	10	6.13	155	0	0.00	149	96.13	6	3.87
Basophils	PRE	163	0	0.00	163	100	0	0.00	159	0	0.00	159	100	0	0.00
	PI(Day 2)	165	0	0.00	164	99.39	1	0.61	158	0	0.00	158	100	0	0.00
	PI(Day 21)	163	0	0.00	163	100	0	0.00	155	0	0.00	155	100	0	0.00
	PII(Day 23)	163	0	0.00	163	100	0	0.00	155	0	0.00	155	100	0	0.00

Creatinine	PRF	165	0	0.00	149	90.30	16	9 70	158	0	0 00	136	86 08	22	13 92
Phosphokinase	Pl(Day 2)	165	0	0.00	150	90.91	15	9.09	158	1	0.63	141	89.24	16	10.02
	Pl(Day 21)	163	1	0.61	140	85.89	22	13 50	156	0	0.00	130	83.33	26	16.10
	PII(Day 23)	163	0	0.00	146	89.57	17	10.00	155	0	0.00	136	87 74	19	12.26
Creatinine	PRF	165	0	0.00	144	87 27	21	12 73	159	0	0.00	148	93.08	11	6.92
oredamine	Pl(Day 2)	165	1	0.61	144	87.27	20	12.12	158	1	0.63	146	92.41	11	6.96
	Pl(Day 21)	163	0	0.00	134	82 21	29	17 79	156	1	0.64	142	91.03	13	8.33
	PII(Day 23)	163	1	0.61	142	87 12	20	12 27	155	1	0.65	139	89.68	15	9.68
Fosinophils	PRF	163	4	2 45	159	97.55	0	0.00	159	5	3 14	153	96.23	1	0.63
	Pl(Day 2)	165	4	2 42	161	97.58	0	0.00	158	5	3 16	152	96.20	1	0.63
	Pl(Day 21)	163	4	2.12	158	96.93	1	0.60	155	4	2.58	150	96 77	1	0.65
	PII(Day 23)	163	4	2.10	159	97.55	0	0.00	155	4	2.58	149	96 13	2	1 29
Haemoglobin	PRF	163	11	6 75	137	84.05	15	9.00	159	14	8.81	130	81 76	15	9.43
ridemoglobin	PI(Day 2)	165	21	12 73	139	84 24	5	3.03	158	16	10 13	135	85.44	7	4 4 3
	PI(Day 21)	163	13	7 98	1//	88 3/	6	3.68	155	15	9.68	130	83.87	10	6.45
	PII(Day 23)	163	20	12 27	130	85 28	1	2.00	155	17	10 07	133	85.81	5	3.23
Lactate		16/	1	0.61	1/7	80.63	16	9.76	156	2	1 28	136	87 18	18	11 5/
Dehydrogenase		165	2	1.01	1/18	80 70	10	0.10 0.00	158	2	1.20	1//	01.10	10	7 50
Denydrogenase	PI(Day 2)	162	2	0.00	140	03.70	10	9.09 6.70	156	2	0.64	1/12	91.14	12	1.09
	PI(Day 21)	162	4	2.45	1/17	93.21	12	7.26	150	י ר	1 20	142	91.03	10	0.33
Lymphopytoc	DDE	163	4	2.45	147	90.10 11.04	12	1.30	150	2 127	1.29	22	12.97	0	0.00
Lymphocytes		165	140	00.90	10	10.20	0	0.00	159	126	00.10	22	12.04	0	0.00
	PI(Day 2)	162	140	09.70	10	11.50	0	0.00	150	130	00.00	22	13.92	0	0.00
	PI(Day 21)	103	144	00.34	19	10.42	1	0.00	155	100	07.10	20	12.90	0	0.00
Managutag	Pli(Day 23)	163	140	00.90	17	10.43		0.01	100	100	01.1U 05.52	20	12.90	0	0.00
Monocytes		103	143	01.13	20	12.27	1	0.00	159	130	00.00	23	14.47	0	0.00
	PI(Day 2)	100	143	00.07	21	12.73		0.01	100	104	04.01	24	12.19	0	0.00
	PI(Day 21)	103	140	00.09	23	14.11	0	0.00	100	134	00.40	21	13.55	0	0.00
Neutronhile	PII(Day 23)	163	141	86.50	19	71.00	3	1.84	155	134	80.45	17	10.97	4	2.58
Neutrophils		103	140	90.80	13	7.98	2	1.23	100	141	09.Z4	17	10.70	0	0.00
	PI(Day 2)	165	149	90.30	13	1.88	3	1.82	158	141	89.24	17	10.76	0	0.00
	PI(Day 21)	103	147	90.18	14	0.59	2	1.23	100	130	09.03	10	9.00	2	1.29
Districts	PII(Day 23)	163	148	90.80	14	8.59	1	0.61	155	138	89.03	1/	10.97	0	0.00
Platelets		163	4	2.45	145	88.96	14	8.59	159	3	1.89	148	93.08	ð 7	5.03
	PI(Day 2)	105	2	1.21	152	92.12	11	0.07	158	4	2.53	147	93.04	1	4.43
	PI(Day 21)	163	3	1.84	147	90.18	13	7.98	155	4	2.58	145	93.55	6	3.87
Ded Dised Oall	PII(Day 23)	163	2	1.23	150	92.02	11	6.75	155	2	1.29	147	94.84	6	3.87
Red Blood Cell	PKE	163	21	12.88	132	80.98	10	0.13	159	21	13.21	125	18.62	13	0.10
count	PI(Day 2)	105	25	15.15	134	81.21	6	3.64	158	20	12.00	133	84.18	5	3.10
	PI(Day 21)	163	24	14.72	133	81.60	6	3.68	155	20	12.90	127	81.94	8	5.16
	PII(Day 23)	163	33	20.25	127	//.91	3	1.84	155	19	12.26	134	86.45	2	1.29
Urea	PRE	165	0	0.00	90	54.55	/5	45.45	159	4	2.52	101	63.52	54	33.96
	PI(Day 2)	164	1	0.61	96	58.54	67	40.85	158	4	2.53	114	72.15	40	25.32
	PI(Day 21)	163	0	0.00	91	55.83	72	44.17	156	3	1.92	100	64.10	53	33.97
	PII(Day 23)	163	0	0.00	105	64.42	58	35.58	155	2	1.29	106	68.39	47	30.32
White Blood Cell	PRE	163	5	3.07	152	93.25	6	3.68	159	3	1.89	155	97.48	1	0.63
count	PI(Day 2)	165	4	2.42	152	92.12	9	5.45	158	4	2.53	152	96.20	2	1.27
	PI(Day 21)	163	4	2.45	150	92.02	9	5.52	155	3	1.94	149	96.13	3	1.94
	PII(Day 23)	163	6	3.68	145	88.96	12	7.36	155	7	4.52	148	95.48	0	0.00
N = number of su n%= number/per PRE = Pre-vacci	ubjects with ava centage of sub nation at Day 0	ilable re jects in th	sults ne spe	cified ca	ategor	у									
PI(Day 2) = Pos	t-vaccination at	Day 2													

PI (Day 21) = Post-vaccination at Day 21 PII (Day 23) = Post-vaccination at Day 23

Secondary Outcome/Efficacy Variables: Number (%) of subjects	with AESIs during the entire	e study period (Total
	LIENIA	Double H5N1
AESIS	Group	Group
	N=165	N=159
Subjects with any AESI(s), n (%)	0 (0.0)	0 (0,0)
Safety results: Number (%) of subjects with unsolicited adverse ex	vents (Total vaccinated coho	rt)
Most frequent adverse events - On-Therapy	H5N1	Double H5N1
(occurring within Day 0- 20 after first vaccination and within	Group	Group
Day 0-29 after second vaccination)	N=165	N=159
Subjects with any AE(s), n (%)	36 (21.8)	28 (17.6)
Subjects with Grade 3 AE(s), n (%)	5 (3.0)	3 (1.9)
Subjects with related AE(s), n (%)	9 (5.5)	10 (6.3)
Diarrhea	3 (1.8)	1 (0.6)
Nausea	2 (1.2)	3 (1.9)
Vertigo	2 (1.2)	1 (0.6)
Tracheitis	4 (2.4)	-
Erythema	2 (1.2)	1 (0.6)
Gastroenteritis	-	1 (0.6)
Injection site pruritus	-	4 (2.5)
Nasopharyngitis	2 (1.2)	-
Rhinitis	2 (1.2)	1 (0.6)
Cough	2 (1.2)	1 (0.6)
Neck pain	-	2 (1.3)
Pain in extremity	3 (1.8)	-
Pharyngitis	-	2 (1.3)
Abdominal pain upper	2 (1.2)	-
Arthralgia	2 (1.2)	-
Lymphadenopathy	-	1 (0.6)
Congestive cardiomyopathy	-	1 (0.6)
Coronary artery disease	-	1 (0.6)
Tachycardia	-	1 (0.6)
Tinnitus	-	1 (0.6)
Cheilitis	-	1 (0.6)
Paraesthesia oral	-	1 (0.6)
loothache	-	1 (0.6)
Fatigue	-	1 (0.6)
Influenza like illness	-	1 (0.6)
Injection site rash	-	1 (0.6)
	-	1 (0.6)
Initializa	-	1 (0.6)
	-	1 (0.0)
Tooth absence	-	1 (0.0)
Back pain	-	1 (0.6)
Muscle snasms	-	1 (0.6)
Asteoarthritis	-	1 (0.6)
Scleroderma	_	1 (0.0)
Paraesthesia	-	1 (0.6)
Sensory disturbance		1 (0.6)
Dvsnnoea	-	1 (0.6)
Rhinitis allergic	-	1 (0.6)
Rhinorrhoea	-	1 (0.6)
-: Adverse event absent or not meeting the counting rule:> 30 subjects and the counting rule:> 30 subj	ects/treatment group and > 3	groups, display the most

frequent 5 events in each treatment group		
*Grade 3 AE: AE that prevented normal activity		
**Related AE: AE assessed by the investigator as causally related to	o the study vaccination	
Safety results: Number (%) of subjects with SAEs between Day 0 a	and Day 51 (Total vaccinated co	hort)
Serious adverse event, n (%) In considered by the investigator	to be related to study medicat	tion1
All SAEs	H5N1	Double H5N1
	Group	Group
	N=165	N=159
Subjects with any SAE(s) n (%) In assessed by investigator as	1 (0 6) [0]	1 (0 6) [0]
related]	(0.0) [0]	1 (0.0) [0]
Coronary artery disease	[0] (0, 0) 0	1 (0.6) [0]
Gastroenteritis	1 (0.6) [0]	0 (0 0) [0]
	H5N1	
	Group	Group
	N=165	N=150
Subjects with fatal SAE(s), $p(\theta')$ in accessed by investigator as		
Subjects with ratal SAE(S), IT (70) [IT assessed by investigator as	0 (0.0) [0]	0 (0.0) [0]
Sefety received	and Day 190 (Tatal yearingted	a a la a stil
Sorieus adverse event n (%) in considered by the investigation		conort)
all CAL		
All SAES	H5N1	Double H5N1
	Group	Group
	N = 164	N = 158
Subjects with any SAE(s), n (%) [n assessed by investigator as	5 (3.0) [0]	5 (3.2) [0]
related		
Cardiac failure congestive	0 (0.0) [0]	1 (0.6) [0]
Adenocarcinoma pancreas	1 (0.6) [0]	0 (0.0) [0]
Atrial fibrillation	1 (0.6) [0]	0 (0.0) [0]
Cardiac failure acute	0 (0.0) [0]	1 (0.6) [0]
Cerebral ischaemia	1 (0.6) [0]	0 (0.0) [0]
Cerebrovascular accident	0 (0.0) [0]	1 (0.6) [0]
Femoral neck fracture	0 (0.0) [0]	1 (0.6) [0]
Cerebral haemorrhage	0 (0.0) [0]	1 (0.6) [0]
Renal cell carcinoma stage unspecified	1 (0.6) [0]	0 (0.0) [0]
Sciatica	1 (0.6) [0]	0 (0.0) [0]
Fatal SAEs	H5N1	Double H5N1
	Group	Group
	N = 164	N = 158
Subjects with fatal SAE(s), n (%) [n assessed by investigator as	0 (0.0) [0]	3 (1.9) [0]
related]		
Cardiac failure congestive	0 (0.0) [0]	1 (0.6) [0]
Cerebrovascular accident	0 (0.0) [0]	1 (0.6) [0]
Cerebral haemorrhage	0 (0,0) [0]	1 (0.6) [0]
Safety results: Number (%) of subjects with SAEs between Month	6 and Month 12 ((Total Vaccina	ted Cohort at Month 12)
Serious adverse event, n (%) In considered by the investigator	to be related to study medica	tion]
All SAFs	H5N1 Group	Double H5N1 Group
	N = 130	N = 125
Subjects with any SAE(s) n (%) In assessed by investigator as	4 (3 1) [0]	3 (2 4) [0]
related]	. (0.1)[0]	ر ۲. ۲) [۵]
Cerebrovascular accident	2 (1 5) [0]	0 (0 0) [0]
	1 (0.8) [0]	
Lower limb fracture		
Lung noonloom molignant		
Prilebilis		I (U.8) [U]
Prostate cancer metastatic	0 (0.0) [0]	1 (0.8) [0]
Schizophrenia	0 (0.0) [0]	1 (0.8) [0]

Fatal SAEs	H5N1 Group N = 130	Double H5N1 Group N = 125
Subjects with fatal SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]
Safety results: Number (%) of subjects with serious adverse events Cohort at Month 24)	between Month 12 and Month	n 24 (Total Vaccinated
Serious adverse event, n (%) [n considered by the investigator	o be related to study medica	ition]
All SAEs	H5N1	Double H5N1
	N = 122	N = 117
Subjects with any SAE(s), n (%) [n assessed by the investigator as re	lated] 9 (7.4) [0]	7 (6.0) [0]
Aortic aneurysm	0 (0.0) [0]	1 (0.9) [0]
Pneumonia	1 (0.8) [0]	0 (0.0) [0]
Acute myocardial infarction	1 (0.8) [0]	0 (0.0) [0]
Angioedema	1 (0.8) [0]	0 (0.0) [0]
Benign prostatic hyperplasia	0 (0.0) [0]	1 (0.9) [0]
Biliary colic	0 (0.0) [0]	1 (0.9) [0]
Bradycardia	1 (0.8) [0]	0 (0.0) [0]
Bronchospasm	1 (0.8) [0]	0 (0.0) [0]
Cardiac failure congestive	0 (0.0) [0]	1 (0.9) [0]
Cerebrovascular accident	0 (0.0) [0]	1 (0.9) [0]
Extrasystoles	1 (0.8) [0]	0 (0.0) [0]
Polyneuropathy	1 (0.8) [0]	0 (0.0) [0]
Prostate cancer	1 (0.8) [0]	0 (0.0) [0]
Pulmonary embolism	1 (0.8) [0]	0 (0.0) [0]
Rectal cancer	1 (0.8) [0]	0 (0.0) [0]
Renal cell carcinoma	1 (0.8) [0]	0 (0.0) [0]
Renal failure	0 (0.0) [0]	1 (0.9) [0]
Venous insufficiency	0 (0.0) [0]	1 (0.9) [0]
Fatal SAEs	H5N1	Double H5N1
	N = 122	N = 117
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]	0 (0.0) [0]

Conclusion: In H5N1 group, at least 18.4% of subjects reported pre-vaccination SPRs for H5N1 HI antibody against the A/Vietnam/1194/2004 strain. At Day 21, 42, 180, Month 12 and 24, 61.2%, 83.6%, 52.9%, 43.8% and 37.2% of the subjects had H5N1 HI antibody titres \geq 1:40 against the A/Vietnam/1194/2004 strain.

At Day 21, 42, 180, Month 12 and 24, 3.3%, 23.0%, 3.6%, 15.2% and 4.7% of the subjects had H5N1 HI antibody titres \geq 1:40 against A/Indonesia/5/2005 strain.

In Double H5N1 group, at least 15.9% of subjects reported pre-vaccination SPRs for H5N1 HI antibody against the A/Vietnam/1194/2004 strain. At Day 21, 42, 180, Month 12 and 24, 62.1%, 95.9%, 69.5%, 42.5% and 30.9% of the subjects had H5N1 HI antibody titres \geq 1:40 against the A/Vietnam/1194/2004 strain.

At Day 21, 42, 180, Month 12 and 24, 9.0%, 40.7 %, 6.1%, 20.8% and 6.2% of the subjects had H5N1 HI antibody titres \geq 1:40 against A/Indonesia/5/2005 strain.

At least one unsolicited AE was reported during the follow-up period after vaccination by 36 (21.8%) subjects of H5N1 group and 28 (17.6%) subjects of Double H5N1 group. From Day 0 up to Day 51, two SAEs were reported (one in each group). None of these SAEs were assessed by the investigators as related to the study vaccination.

Between Day 51 and Day 180, SAEs were reported for 5 (3.0%) subjects of H5N1 group and 5 (3.2%) subjects of Double H5N1 group. Three fatal SAEs were reported in Double H5N1 group during the entire study period. None of the reported SAEs were assessed by the investigators as related to the study vaccination.

Between Month 6 and Month 12, SAEs were reported for 4 (3.1%) subjects of H5N1 group and 3 (2.4%) subjects of Double H5N1 group. None of the reported SAEs were assessed by the investigators as related to the study vaccination. No fatal SAEs were reported between Month 6 and Month 12.

Between Month 12 and Month 24, SAEs were reported for 7 (6.0%) subjects of Double H5N1 group and 9 (7.4%) subjects of H5N1 Group. None of the reported SAEs were assessed by the investigators as related to the study vaccination. No fatal SAEs were reported between Month 6 and Month 12.

Publications:

Heijmans S et al. (2011) Immunogenicity profile of a 3.75-µg hemagglutinin pandemic rH5N1 split virion AS03A-adjuvanted vaccine in elderly persons: a randomized trial. J Infect Dis. 203(8):1054-1062.

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