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Protocol Registration and Results System

ID: V87P13 Safety, Tolerability and Immunogenicity of Two Doses of Adjuvanted Monovalent Influenza Vaccine Administered to Healthy Adult and Elderly Subjects NCT00841763

Protocol Registration and Results Preview

Safety, Tolerability and Immunogenicity of Two Doses of Adjuvanted Monovalent Influenza Vaccine Administered to Healthy Adult and Elderly Subjects

This study has been completed.

Sponsor:
Novartis

Collaborators:
Novartis Vaccines

Information provided by (Responsible Party):
Novartis

ClinicalTrials.gov Identifier:
NCT00841763

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Purpose

The present study, phase III, randomized, controlled, observer-blind, multicenter study, will evaluate safety, tolerability and immunogenicity of two doses of an adjuvanted monovalent influenza vaccine compared with an adjuvanted interpandemic trivalent influenza vaccine in a population of healthy adult and elderly subjects.

Condition	Intervention	Phase
Pandemic Influenza Disease	Biological/Vaccine: Placebo (PL) Biological/Vaccine: Trivalent influenza virus vaccine (TIV) Biological/Vaccine: Adjuvanted monovalent influenza virus vaccine (aH5N1) Biological/Vaccine: Adjuvanted trivalent influenza virus vaccine (aTIV)	Phase 3

Study Type: Interventional
Study Design: Prevention, Parallel Assignment, Double Blind (Subject, Investigator), Randomized, Safety Study

Official Title: A Phase III, Randomized, Controlled, Observer-blind, Multicenter Study to Evaluate the Safety, Tolerability and Immunogenicity of Two Doses of a Monovalent A/H5N1 Influenza Vaccine Adjuvanted With MF59 (Fluad-H5N1) in Adult and Elderly Subjects

Further study details as provided by Novartis:

Primary Outcome Measure:

- Number of Subjects With at Least One Reactogenicity Sign After Two Doses of the Adjuvanted Pandemic Influenza Vaccine. [Time Frame: Up to 6 days after each vaccination.] [Designated as safety issue: No]

  To assess the safety and tolerability profile of two doses of the MF59-adjuvanted A/Vietnam/1194/2004 pandemic influenza vaccine (aH5N1), each containing 7.5 µg of H5N1 antigen in terms of the number of participants who reported local and systemic reactions up to 6 days after each vaccination per vaccination group.

- Number of Subjects Exposed to Adjuvanted Pandemic Influenza Vaccine. [Time Frame: Upto Day 224 post vaccination] [Designated as safety issue: No]

  To report safety data from a large enough number of subjects exposed to adjuvanted pandemic influenza vaccine aH5N1 capable of detecting rare adverse events (AEs), i.e. events occurring at a frequency of <=0.1%, & uncommon AEs in elderly, i.e. occurring at a frequency of <=1% of subjects.

Secondary Outcome Measures:

- The Number of Subjects With at Least One Reactogenicity Sign After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine as Compared With the Adjuvanted Seasonal Trivalent Influenza Vaccine aTIV. [Time Frame: Up to 6 days after each vaccination.] [Designated as safety issue: No]

  To evaluate the safety and tolerability profile of two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1) as compared with the MF59-adjuvanted seasonal trivalent influenza vaccine (aTIV), in terms of the number of subjects who reported local and systemic reactions up to 6 days after each vaccination per vaccination group.

- Geometric Mean Titers (GMTs) After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Homologous A/Vietnam/1194/2004 Strain. [Time Frame: Day 22, Day 43, Day 64] [Designated as safety issue: No]

  To evaluate the immunogenicity of two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1), each containing 7.5µg of H5N1 antigen,in terms of GMTs against the homologous A/Vietnam/1194/2004 strain, as determined by Hemagglutination Inhibition (HI) assay and Microneutralization (MN) assay.

- Geometric Mean Areas (GMAs) After Two Doses of the Adjuvanted Pandemic Vaccine (aH5N1). [Time Frame: Day 22, Day 43, Day 64] [Designated as safety issue: No]

  To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine aH5N1, in terms of GMAs as determined by Single Radial Hemolysis (SRH) assay. GMA: For each vaccine group, least squares GMAs (for SRH data), associated 2-sided 95% confidence interval and median, minimal, and maximal titer values were determined for study Day 22, Day 43 and Day 64.

- Geometric Mean Ratios (GMRs) After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Homologous A/Vietnam/1194/2004 Strain. [Time Frame: Day 43/Day 22, Day 64/Day 22] [Designated as safety issue: No]
  To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine (aH5N1), each containing 7.5µg of H5N1 antigen,in terms of GMRs against the homologous A/Vietnam/1194/2004 strain, as determined by HI, MN and SRH assays.

- Percentages of Subjects With HI Titers ≥ 40 and GMAs ≥ 25mm^2, After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Homologous A/Vietnam/1194/2004 Strain. [Time Frame: Day 22, Day 43 and Day 64] [Designated as safety issue: No]
  To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine aH5N1, each containing 7.5µg of H5N1 antigen, against the homologous A/Vietnam/1194/2004 strain, in terms of percentages of subjects achieving HI titers ≥ 40 and GMAs ≥ 25mm^2, as determined by HI and SRH assays. GMA: For each vaccine group, least squares GMAs (for SRH data), associated 2-sided 95% confidence interval and median, minimal, and maximal titer values were determined for study Day 22, Day 43 and Day 64.

- Percentages of Subjects Achieving Seroconversion or Significant Increase in Antibody Titer After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Homologous A/Vietnam/1194/2004 Strain. [Time Frame: Day 43/Day 22 and Day 64/Day 22] [Designated as safety issue: No]
  To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine aH5N1, each containing 7.5µg of H5N1 antigen, against the homologous A/Vietnam/1194/2004 strain, in terms of percentages of subjects achieving seroconversion or significant increase in antibody titer as measured by HI and SRH assays.

- GMTs After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Heterologous A/Turkey/Turkey/1/2005 Strain. [Time Frame: Day 22, Day 43 and Day 64] [Designated as safety issue: No]
  To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine (aH5N1), each containing 7.5µg of H5N1 antigen, in terms of GMTs against the heterologous A/turkey/Turkey/1/2005 strain, as determined by HI and MN assays.

- GMAs After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Heterologous A/Turkey/Turkey/1/2005 Strain. [Time Frame: Day 22, Day 43 and Day 64] [Designated as safety issue: No]
  To evaluate the immunogenicity of two doses of adjuvanted pandemic vaccine aH5N1, each containing 7.5µg of H5N1 antigen, in terms of GMAs against the heterologous A/turkey/Turkey/1/2005 strain, as determined by SRH assay. GMA: For each vaccine group, least squares GMAs (for SRH data), associated 2-sided 95% confidence interval and median, minimal, and maximal titer values were determined for study Day 22, Day 43 and Day 64.

- GMRs After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Heterologous A/Turkey/Turkey/1/2005 Strain. [Time Frame: Day 43/Day 22 and Day 64/Day 22] [Designated as safety issue: No]
  To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine aH5N1, each containing 7.5µg of H5N1 antigen, in terms of GMRs against the heterologous A/turkey/Turkey/1/2005 strain, as determined by HI, MN and SRH assays.

- Percentages of Subjects With HI ≥ 40 and GMAs ≥ 25mm^2, After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Heterologous A/Turkey/Turkey/1/2005 Strain. [Time Frame: Day 22, Day 43 and Day 64] [Designated as safety issue: No]
  To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine aH5N1, each containing 7.5µg of H5N1 antigen, against the heterologous A/turkey/Turkey/1/2005 strain, in terms of percentages of subjects achieving HI titers ≥ 40 and GMAs ≥ 25mm^2 as determined by HI and SRH assays. GMA: For each vaccine group, least squares GMAs (for SRH data), associated 2-sided 95% confidence interval and median, minimal, and maximal titer values were determined for study Vaccine on Day 22, Day 43, Day 64.

- Percentages of Subjects Achieving Seroconversion or Significant Increase in Antibody Titers, After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Heterologous A/Turkey/Turkey/1/2005 Strain. [Time Frame: Day 43/Day 22 and Day 64/Day 22)] [Designated as safety issue: No]
  To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine aH5N1, each containing 7.5µg of H5N1 antigen, against the heterologous A/turkey/Turkey/1/2005 strain, in terms of percentages of subjects achieving seroconversion or significant increase in antibody titer as measured by HI and SRH assays.

- Percentages of Subjects With MN Titers ≥20, ≥40, ≥80, After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Homologous A/Vietnam/1194/2004 Strain. [Time Frame: Day 22, Day 43 and Day 64] [Designated as safety issue: No]
  To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine (aH5N1), each containing 7.5µg of H5N1 antigen, against the homologous A/Vietnam/1194/2004 strain, in terms of percentages of subjects achieving MN Titers ≥20, ≥ 40, ≥80 on Days 22, Day 43 and Day 64.

- Percentages of Subjects With MN Titers ≥20, ≥40, ≥80, After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Heterologous A/Turkey/Turkey/1/2005 Strain. [Time Frame: Day 22, Day 43 and Day 64] [Designated as safety issue: No]
  To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine aH5N1, each containing 7.5µg of H5N1 antigen, against the heterologous A/turkey/Turkey/1/2005 Strain, in terms of percentages of subjects achieving MN Titers ≥20, ≥ 40, ≥80 on Day 22, Day 43 and Day 64.

- Percentages of Subjects Achieving at Least a Four-fold Rise in MN Antibody Titer on Day 43 and Day 64, Compared to Day 22 Against Homologous Strains. [Time Frame: Day 43/Day 22 and Day 64/Day 22] [Designated as safety issue: No]
  To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine aH5N1, each containing 7.5µg of H5N1 antigen, against the homologous A/Vietnam/1194/2004 strain, in terms of percentages of subjects achieving at least a four-fold rise in MN antibody titer on Day 43 and Day 64, compared to Day 22.

- Percentages of Subjects Achieving at Least a Four-fold Rise in MN Antibody Titer on Day 43 and Day 64, Compared to Day 22 Against Heterologous Strains. [Time Frame: Day 43/Day 22 and Day 64/Day 22] [Designated as safety issue: No]
  To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine (aH5N1), each containing 7.5µg of H5N1 antigen, against Heterologous A/turkey/Turkey/1/2005 Strain, in terms of percentages of subjects achieving at least a four-fold rise in MN antibody titer on Day 43 and Day 64, compared to Day 22.

- Number of Subjects Reporting Unsolicited AEs After Vaccination. [Time Frame: Day 1 through Day 224 post vaccination] [Designated as safety issue: No]
  The number of subjects reporting any unsolicited AEs any, Possibly/probably related AEs, serious adverse events (SAEs), AEs leading to withdrawal (WD), AEs leading to death from Day 1 through Day 224 post vaccination.

Enrollment: 3647
Study Start Date: October 2008
Study Completion Date: November 2009
Primary Completion Date: April 2009

Arms	Assigned Interventions
Experimental: TIV + aH5N1 First dose of the non-adjuvanted trivalent influenza virus vaccine (TIV) followed by two doses of the adjuvanted monovalent influenza virus vaccine (aH5N1).	Biological/Vaccine: Trivalent influenza virus vaccine (TIV) A single IM injection of a 0.5 ml dose of non-adjuvanted trivalent influenza virus vaccine administered in the deltoid muscle, preferably of the non-dominant arm. Biological/Vaccine: Adjuvanted monovalent influenza virus vaccine (aH5N1) Two intramuscular (IM) injections of a 0.5 ml dose administered three weeks apart in the deltoid muscle.
Active Comparator: PL + aTIV First dose of placebo (PL-saline) followed by two doses of the adjuvanted trivalent influenza virus vaccine (aTIV).	Biological/Vaccine: Placebo (PL) One dose of 0.5 ml IM injection of isotonic saline solution was administered in the deltoid muscle, preferably of the non-dominant arm. Biological/Vaccine: Adjuvanted trivalent influenza virus vaccine (aTIV) Two IM injections of a 0.5 ml dose of adjuvanted trivalent influenza virus vaccine administered three weeks apart, in the deltoid muscle.

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts healthy volunteers.
Inclusion Criteria:

- Subjects 18 years of age and older who were mentally competent and who had signed an informed consent form after having received a detailed explanation of the study protocol;
- In good health as determined by:
    a. medical history,
    b. physical examination,
    c. clinical judgment of the Investigator;
- Able to understand and comply with all study procedures and to complete study diaries, could be contacted, and were available for study visits;

Exclusion Criteria:

- Receipt of another investigational agent within 4 weeks;
- Laboratory-confirmed influenza disease within 6 months prior to Visit 1;
- Receipt of influenza vaccination for current season 2008/2009;
- Experienced any acute disease or infection requiring systemic antibiotic or antiviral therapy (chronic antibiotic therapy for urinary tract prophylaxis was acceptable) within the past 7 days;
- Experienced fever (defined as axillary temperature ≥38.0°C) within 7 days prior to Visit 1;
- Pregnant or breastfeeding;
- Females of childbearing potential who were sexually active and had not used or did not plan or refused to use an acceptable method of birth control during the active phase of the study (at least up to three weeks after last vaccine injection);
- Any serious disease, such as: cancer, autoimmune disease (including rheumatoid arthritis); diabetes mellitus type I and type II; diabetes relating to genetic defects/syndromes, diseases of the exocrine pancreas or infections; advanced arteriosclerotic disease; severe chronic obstructive pulmonary disease (COPD), i.e. GOLD stages 3 and 4; acute or progressive hepatic disease and renal disease; congestive heart failure; Body Mass Index (BMI) ≥35 kg/m2 where BMI reflects obesity and not high muscle mass;
- History of progressive or severe neurologic disorders, of any neurological symptoms or signs, or anaphylactic shock following administration of any study vaccine;
- Bleeding diathesis;
- Surgery planned during the study period;
- Hypersensitivity to eggs, chicken protein, chicken feathers, influenza viral protein, neomycin or polymyxin or any other component of the study vaccines;
- Known or suspected impairment/alteration of immune function, for example, resulting from:
    a. receipt of immunosuppressive therapy (any corticosteroid therapy or cancer chemotherapy) or other immunosuppressive agents within the past 60 days and for the full length of the study;
    b. receipt of immunostimulants;
    c. receipt of parenteral immunoglobulin preparation, blood products and/or plasma derivates within the past 3 months and for the full length of the study;

d. suspected or known HIV infection or HIV-related disease;

- Receipt of non study vaccines (with the exception of post-exposure vaccination in a medical emergency, e.g. hepatitis, rabies, tetanus) within 3 weeks prior to Visit 1 or planned vaccination within 3 weeks following the last study vaccination;
- History of (or current) drug or alcohol abuse that in the investigator's opinion would interfere with safety of the subject or the evaluation of study objectives;
- Members of research staff and their relatives;
- Any condition, which, in the opinion of the Investigator, might interfere with the evaluation of the study objectives.

Contacts and Locations

Locations

Finland

Tampere Vaccine Research Clinic (15 sites)

Tampere, Finland, 33100

Germany

12 Sites

München, Germany, 80799

Investigators

Study Director: Novartis Vaccines Novartis Vaccines and Diagnostics

More Information

Results Publications:

Vesikari T, Forstén A, Herbinger KH, Cioppa GD, Beygo J, Borkowski A, Groth N, Bennati M, von Sonnenburg F. Safety and immunogenicity of an MF59(®)-adjuvanted A/H5N1 pre-pandemic influenza vaccine in adults and the elderly. Vaccine. 2012 Feb 8;30 (7):1388-96. doi: 10.1016/j.vaccine.2011.12.009. Epub 2011 Dec 20.

Responsible Party: Novartis

Study ID Numbers: V87P13
2008-003871-32

Health Authority: Germany: Paul-Ehrlich-Institut

Study Results

Participant Flow

Recruitment Details	Subjects were enrolled from 27 centers across Finland and Germany.
Pre-Assignment Details	All subjects enrolled were included in the trial.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs)	PL+ aTIV (18-60 Yrs)	TIV + aH5N1 (>60 Yrs)	PL+ aTIV (>60 Yrs)	Total (Not public)
Arm/Group Description	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of placebo (PL) followed by two doses of adjuvanted seasonal trivalent influenza vaccine (aTIV).	First dose of non adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 influenza vaccine (aH5N1).	First dose of placebo (PL) followed by two doses of adjuvanted seasonal trivalent influenza vaccine (aTIV).	
Period Title: **Overall Study**					
Started	2691	681	219	56	3647
Completed	2529	624	211	53	3417
Not Completed	162	57	8	3	230
Reason Not Completed					
Withdrawal by Subject	60	17	4	1	82
Adverse Event	9	10	3	2	24
Lost to Follow-up	63	25	0	0	88
Protocol Violation	20	3	1	0	24
Administrative Reasons	3	1	0	0	4
Unable to Classify	7	1	0	0	8
(Not Public)	Not Completed = 162 Total from all reasons = 162	Not Completed = 57 Total from all reasons = 57	Not Completed = 8 Total from all reasons = 8	Not Completed = 3 Total from all reasons = 3	

Baseline Characteristics

Arm/Group Title	TIV + aH5N1	PL+ aTIV	Total
Arm/Group Description	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of placebo (PL) followed by two doses of adjuvanted seasonal trivalent influenza vaccine (aTIV).	
Overall Number of Baseline Participants	2911	735	**3646**
Baseline Analysis Population Description [Not specified]			
Age, Customized [1] Mean (Standard Deviation) Units: Years			
<= 60 years (N= 2692, 679)	40.7 (11.6)	40.5 (12.0)	40.7 (11.7)
>60 years (N= 219, 56)	61.9 (1.4)	62.1 (1.8)	61.9 (1.5)
	[1] The number of subjects analyzed is not consistent with the Participant Flow module due to randomization errors. The enrolled set as randomized is reported in the Participant Flow Module but in the Baseline Measure module, the enrolled set as treated is reported (2 randomization errors so 2 subjects were changed from the TIV + aH5N1 group to the PL+ aTIV group). Moreover, a subset to the enrolled population as treated excluded the one subject who was not vaccinated.		
Gender, Customized Measure Type: Number Units: Subjects			
Female (<=60 yrs)	1502	388	1890
Male (<=60 yrs)	1190	291	1481
Female (>60 yrs; N= 109; 28)	109	28	137
Male (>60 yrs; N= 110, 28)	110	28	138

Outcome Measures

1. Primary Outcome

Title:	Number of Subjects With at Least One Reactogenicity Sign After Two Doses of the Adjuvanted Pandemic Influenza Vaccine.
▼ Description:	To assess the safety and tolerability profile of two doses of the MF59-adjuvanted A/Vietnam/1194/2004 pandemic influenza vaccine (aH5N1), each containing 7.5 µg of H5N1 antigen in terms of the number of participants who reported local and systemic reactions up to 6 days after each vaccination per vaccination group.
Time Frame:	Up to 6 days after each vaccination.
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

The analysis was performed on the Safety Set population.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs)	PL+ aTIV (18-60 Yrs)
▼ Arm/Group Description:	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of placebo (PL) followed by two doses of adjuvanted seasonal trivalent influenza vaccine (aTIV).
Number of Participants Analyzed	2611	658
Measure Type: Number Units: Participants		
Local reactions	1755	502
Injection site ecchymosis (N= 2610,214)	237	78
Injection site erythema (N= 2610,214)	652	206
Injection site induration (N= 2610,214)	549	181
Injection site swelling (N= 2610,214)	409	162
Injection site pain (N= 2610,214)	1537	448
Systemic reactions	1387	386
Chills (N= 2610,214)	342	118

Malaise (N= 2610,214)	347	130
Myalgia (N= 2610,214)	869	277
Arthralgia (N= 2610,214)	188	79
Nausea (N= 2610,214)	193	64
Headache (N= 2610,214)	668	189
Sweating (N= 2610,214)	237	658
Fatigue (N= 2610,214)	638	188
Fever ≥ 38°C (N= 2610,214)	28	12
Stayed at home (N= 2591,214)	64	22
Analgesic Antipyretic medi. used (N= 2608,214)	361	114

2. Primary Outcome

Title:	Number of Subjects Exposed to Adjuvanted Pandemic Influenza Vaccine.
▼ Description:	To report safety data from a large enough number of subjects exposed to adjuvanted pandemic influenza vaccine aH5N1 capable of detecting rare adverse events (AEs), i.e. events occurring at a frequency of <=0.1%, & uncommon AEs in elderly, i.e. occurring at a frequency of <=1% of subjects.
Time Frame:	Upto Day 224 post vaccination
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

The analysis was performed on the Safety set population.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs)	PL+ aTIV (18-60 Yrs)	TIV + aH5N1 (>60 Yrs)	PL+ aTIV (>60 Yrs)
▼ Arm/Group Description:	First dose of non-adjuvanted seasonal trivalent influenza	First dose of placebo (PL) followed by two doses of adjuvanted	First dose of non adjuvanted seasonal trivalent influenza	First dose of placebo (PL) followed by two doses of adjuvanted

	vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	seasonal trivalent influenza vaccine (aTIV).	vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 influenza vaccine (aH5N1).	seasonal trivalent influenza vaccine (aTIV).
Number of Participants Analyzed	2693	679	219	56
Measure Type: Number Units: Participants	2692	679	219	56

3. Secondary Outcome

Title:	The Number of Subjects With at Least One Reactogenicity Sign After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine as Compared With the Adjuvanted Seasonal Trivalent Influenza Vaccine aTIV.
▼ Description:	To evaluate the safety and tolerability profile of two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1) as compared with the MF59-adjuvanted seasonal trivalent influenza vaccine (aTIV), in terms of the number of subjects who reported local and systemic reactions up to 6 days after each vaccination per vaccination group.
Time Frame:	Up to 6 days after each vaccination.
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description
The analysis was performed on the Safety set population.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs)	PL+ aTIV (18-60 Yrs)	TIV + aH5N1 (>60 Yrs)	PL+ aTIV (>60 Yrs)
▼ Arm/Group Description:	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of placebo (PL) followed by two doses of adjuvanted seasonal trivalent influenza vaccine (aTIV).	First dose of non adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 influenza vaccine (aH5N1).	First dose of placebo (PL) followed by two doses of adjuvanted seasonal trivalent influenza vaccine (aTIV).

Number of Participants Analyzed	2611	658	214	54
Measure Type: Number Units: Subjects				
Local reactions	1755	502	115	30
Injection site ecchymosis (N= 2610,658,214,54)	237	78	23	7
Injection site erythema (N= 2610,658,214,54)	652	206	45	14
Injection site induration (N= 2610,658,214,54)	549	181	22	10
Injection site swelling (N= 2610,658,214,54)	409	162	22	6
Injection site pain (N= 2610,658,214,54)	1537	448	87	21
Systemic reactions	1387	386	95	26
Chills (N= 2610,658,214,54)	342	118	29	10
Malaise (N= 2610,658,214,54)	347	130	25	6
Myalgia (N= 2610,658,214,54)	869	277	59	16
Arthralgia (N= 2610,658,214,54)	188	79	15	5
Nausea (N= 2610,658,214,54)	193	64	14	3
Headache (N= 2610,658,214,54)	668	189	38	10
Sweating (N= 2610,658,214,54)	237	63	10	2
Fatigue (N= 2610,658,214,54)	638	188	27	7
Fever ≥38°C (N= 2610,658,214,54)	28	12	1	1
	64	22	3	1

Stayed at home (N= 2591,651,214,54)				
Analg. Antipyr. Medi. used (N= 2608,658,214,54)	361	114	27	6

4. Secondary Outcome

Title:	Geometric Mean Titers (GMTs) After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Homologous A/Vietnam/1194/2004 Strain.
▼ Description:	To evaluate the immunogenicity of two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1), each containing 7.5µg of H5N1 antigen,in terms of GMTs against the homologous A/Vietnam/1194/2004 strain, as determined by Hemagglutination Inhibition (HI) assay and Microneutralization (MN) assay.
Time Frame:	Day 22, Day 43, Day 64
Safety Issue?	No

▼ Outcome Measure Data ✔

▼ Analysis Population Description

The analysis was performed on the Full Analysis Set (FAS) of the Immunogenicity Subset - All subjects in the enrolled population who were in the immunogenicity subset and who actually received at least one dose of AdjPanH5N1 or Adj Seasonal, and provided at leasr one evaluable serum sample both before and after baseline.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs) HI Assay	TIV + aH5N1 (>60 Yrs) HI Assay	TIV + aH5N1 (18-60 Yrs) MN Assay	TIV + aH5N1 (>60 Yrs) MN Assay
▼ Arm/Group Description:	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1)	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).
Number of Participants Analyzed	196	205	197	209
Geometric Mean (95% Confidence Interval)				

Units: Titers				
Day 22 (baseline)	6.17 (5.58 to 6.83)	6.98 (6.21 to 7.85)	11 (10 to 11)	10 (9.97 to 11)
Day 43 (N= 196,201,197,207)	14 (11 to 17)	15 (12 to 18)	17 (15 to 19)	17 (15 to 19)
Day 64 (N= 195,203,197,208)	44 (34 to 56)	36 (28 to 45)	65 (56 to 77)	45 (39 to 53)

5. Secondary Outcome

Title:	Geometric Mean Areas (GMAs) After Two Doses of the Adjuvanted Pandemic Vaccine (aH5N1).
▼ Description:	To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine aH5N1, in terms of GMAs as determined by Single Radial Hemolysis (SRH) assay. GMA: For each vaccine group, least squares GMAs (for SRH data), associated 2-sided 95% confidence interval and median, minimal, and maximal titer values were determined for study Day 22, Day 43 and Day 64.
Time Frame:	Day 22, Day 43, Day 64
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

The analysis was performed on FAS population.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs)	TIV + aH5N1 (>60 Yrs)
▼ Arm/Group Description:	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).
Number of Participants Analyzed	197	210
Geometric Mean (95% Confidence Interval) Units: Areas (mm^2)		
Day 22 (baseline)	11 (9.45 to 12)	13 (11 to 14)
Day 43 (N= 197,208)	21 (18 to 24)	20 (18 to 23)
Day 64 (N= 197,209)	43 (39 to 47)	37 (33 to 41)

6. Secondary Outcome

Title:	Geometric Mean Ratios (GMRs) After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Homologous A/Vietnam/1194/2004 Strain.
Description:	To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine (aH5N1), each containing 7.5µg of H5N1 antigen,in terms of GMRs against the homologous A/Vietnam/1194/2004 strain, as determined by HI, MN and SRH assays.
Time Frame:	Day 43/Day 22, Day 64/Day 22
Safety Issue?	No

Outcome Measure Data

Analysis Population Description

The analysis was performed on FAS population.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs) HI Assay	TIV + aH5N1 (>60 Yrs) HI Assay	TIV + aH5N1 (18-60 Yrs) MN Assay	TIV + aH5N1 (>60 Yrs) MN Assay	TIV + aH5N1 (18-60 Yrs) SRH Assay	TIV + aH5N1 (>60 Yrs) SRH Assay
Arm/Group Description:	First dose of the non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of the non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of the non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of the non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).
Number of Participants Analyzed	196	203	197	208	197	209
Geometric Mean (95% Confidence Interval) Units: Ratios						

Day 43 to Day 22 (N= 196,201,197,207,197,208)	2.25 (1.86 to 2.72)	2.14 (1.8 to 2.54)	1.58 (1.39 to 1.79)	1.63 (1.43 to 1.84)	1.95 (1.72 to 2.2)	1.57 (1.41 to 1.75)
Day 64 to Day 22 (N= 195,203,197,208,197,209)	7.1 (5.52 to 9.14)	5.15 (4.15 to 6.4)	6.21 (5.29 to 7.29)	4.42 (3.79 to 5.15)	4.03 (3.54 to 4.59)	2.9 (2.53 to 3.31)

7. Secondary Outcome

Title:	Percentages of Subjects With HI Titers ≥ 40 and GMAs ≥ 25mm^2, After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Homologous A/Vietnam/1194/2004 Strain.
▼ Description:	To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine aH5N1, each containing 7.5µg of H5N1 antigen, against the homologous A/Vietnam/1194/2004 strain, in terms of percentages of subjects achieving HI titers ≥ 40 and GMAs ≥ 25mm^2, as determined by HI and SRH assays. GMA: For each vaccine group, least squares GMAs (for SRH data), associated 2-sided 95% confidence interval and median, minimal, and maximal titer values were determined for study Day 22, Day 43 and Day 64.
Time Frame:	Day 22, Day 43 and Day 64
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

The analysis was performed on FAS population.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs) HI Titers ≥ 40	TIV + aH5N1 (>60 Yrs) HI Titers ≥ 40	TIV + H5N1 (18-60 Yrs) SRH Areas ≥ 25mm^2	TIV + aH5N1 (>60 Yrs) SRH Areas ≥ 25mm^2
▼ Arm/Group Description:	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic vaccine (aH5N1).	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).
Number of Participants Analyzed	196	205	197	210
Number (95% Confidence Interval)				

Units: Percentages of subjects				
Day 22 (baseline)	6 (3 to 10)	8 (5 to 12)	19 (14 to 26)	25 (20 to 32)
Day 43 (N= 196,201,197,208)	30 (23 to 37)	31 (25 to 38)	48 (41 to 55)	46 (39 to 53)
Day 64 (N= 195,203,197,209)	61 (53 to 67)	57 (50 to 64)	91 (87 to 95)	82 (76 to 87)

8. Secondary Outcome

Title:	Percentages of Subjects Achieving Seroconversion or Significant Increase in Antibody Titer After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Homologous A/Vietnam/1194/2004 Strain.
▼ Description:	To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine aH5N1, each containing 7.5µg of H5N1 antigen, against the homologous A/Vietnam/1194/2004 strain, in terms of percentages of subjects achieving seroconversion or significant increase in antibody titer as measured by HI and SRH assays.
Time Frame:	Day 43/Day 22 and Day 64/Day 22
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description
The analysis was performed on FAS population.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs) HI Titers	TIV + aH5N1 (>60 Yrs) HI Titers	TIV + aH5N1 (18-60 Yrs) SRH Areas	TIV + aH5N1 (>60 Yrs) SRH Areas
▼ Arm/Group Description:	First dose of the non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of the non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of the adjuvanted pandemic H5N1 vaccine (H5N1).	First dose of the non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of the non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1).
Number of Participants Analyzed	196	203	197	209
Number (95% Confidence Interval)				

Units: Percentages of subjects				
Day 43/Day 22 (N= 196,201,197,207,197,208)	23 (18 to 30)	22 (16 to 28)	37 (30 to 44)	23 (17 to 29)
Day 64/Day 22 (N= 195,203,197,208,197,209)	56 (49 to 63)	50 (43 to 57)	78 (72 to 84)	63 (56 to 69)

9. Secondary Outcome

Title:	GMTs After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Heterologous A/Turkey/Turkey/1/2005 Strain.
▼ Description:	To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine (aH5N1), each containing 7.5µg of H5N1 antigen, in terms of GMTs against the heterologous A/turkey/Turkey/1/2005 strain, as determined by HI and MN assays.
Time Frame:	Day 22, Day 43 and Day 64
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description
The analysis was performed on FAS population.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs) HI Assay	TIV + aH5N1 (>60 Yrs) HI Assay	TIV + aH5N1 (18-60 Yrs) MN Assay	TIV + aH5N1 (>60 Yrs) MN Assay
▼ Arm/Group Description:	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non-adjuvanted seasonal trivalent influenza vaccine (eTIV_a) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).
Number of Participants Analyzed	197	208	197	210
Geometric Mean (95% Confidence Interval) Units: Titers				

Day 22 (baseline)	6.03 (5.55 to 6.55)	6.85 (6.21 to 7.55)	11 (10 to 11)	11 (11 to 12)
Day 43 (N= 197,206,196,207)	8.03 (7.07 to 9.12)	8.87 (7.69 to 10)	15 (13 to 17)	15 (13 to 16)
Day 64 (N= 197,207,197,208)	12 (9.77 to 14)	12 (10 to 14)	30 (26 to 35)	23 (20 to 26)

10. Secondary Outcome

Title:	GMAs After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Heterologous A/Turkey/Turkey/1/2005 Strain.
▼ Description:	To evaluate the immunogenicity of two doses of adjuvanted pandemic vaccine aH5N1, each containing 7.5µg of H5N1 antigen, in terms of GMAs against the heterologous A/turkey/Turkey/1/2005 strain, as determined by SRH assay. GMA: For each vaccine group, least squares GMAs (for SRH data), associated 2-sided 95% confidence interval and median, minimal, and maximal titer values were determined for study Day 22, Day 43 and Day 64.
Time Frame:	Day 22, Day 43 and Day 64
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description
The analysis was performed on FAS population.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs)	TIV + aH5N1 (>60 Yrs)
▼ Arm/Group Description:	First dose of the non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of the non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1).
Number of Participants Analyzed	197	210
Geometric Mean (95% Confidence Interval) Units: Areas (mm^2)		
Day 22 (baseline)	9.89 (8.82 to 11)	12 (10 to 13)
Day 43 (N= 196,208)	14 (13 to 16)	14 (13 to 16)

Day 64 (N= 197,209)	23 (21 to 26)	20 (18 to 23)

11. Secondary Outcome

Title:	GMRs After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Heterologous A/Turkey/Turkey/1/2005 Strain.
Description:	To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine aH5N1, each containing 7.5µg of H5N1 antigen, in terms of GMRs against the heterologous A/turkey/Turkey/1/2005 strain, as determined by HI, MN and SRH assays.
Time Frame:	Day 43/Day 22 and Day 64/Day 22
Safety Issue?	No

Outcome Measure Data

Analysis Population Description

The analysis was performed on FAS population.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs) HI Assay	TIV + aH5N1 (>60 Yrs) HI Assay	TIV + aH5N1 (18-60 Yrs) MN Assay	TIV + aH5N1 (>60 Yrs) MN Assay	TIV + aH5N1 (18-60 Yrs) SRH Assay	TIV + aH5N1 (>60 Yrs) SRH Assay
Arm/Group Description:	First dose of the non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of the non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of the non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of the non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of the non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of the non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of the adjuvanted pandemic H5N1 vaccine (aH5N1).
Number of Participants Analyzed	197	207	197	208	197	209

Geometric Mean (95% Confidence Interval) Units: Ratios						
Day 43/Day 22 (N=197,206,196,207,196,208)	1.33 (1.19 to 1.49)	1.29 (1.16 to 1.45)	1.39 (1.25 to 1.54)	1.29 (1.17 to 1.42)	1.44 (1.31 to 1.59)	1.25 (1.15 to 1.36)
Day 64/Day 22 (N=197,207,197,208,197,209)	1.92 (1.64 to 2.25)	1.79 (1.56 to 2.06)	2.77 (2.4 to 3.2)	2.01 (1.78 to 2.26)	2.37 (2.1 to 2.67)	1.74 (1.57 to 1.94)

12. Secondary Outcome

Title:	Percentages of Subjects With HI ≥ 40 and GMAs ≥ 25mm^2, After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Heterologous A/Turkey/Turkey/1/2005 Strain.
▼ Description:	To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine aH5N1, each containing 7.5µg of H5N1 antigen, against the heterologous A/turkey/Turkey/1/2005 strain, in terms of percentages of subjects achieving HI titers ≥ 40 and GMAs ≥ 25mm^2 as determined by HI and SRH assays. GMA: For each vaccine group, least squares GMAs (for SRH data), associated 2-sided 95% confidence interval and median, minimal, and maximal titer values were determined for study Vaccine on Day 22, Day 43, Day 64.
Time Frame:	Day 22, Day 43 and Day 64
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

The analysis was performed on FAS population.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs) HI Titers ≥ 40	TIV + aH5N1 (>60 Yrs) HI Titers ≥ 40	TIV + aH5N1 (18-60 Yrs) SRH Areas ≥ 25mm^2	TIV + aH5N1 (>60 Yrs) SRH Areas≥ 25mm^2
▼ Arm/Group Description:	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).

Number of Participants Analyzed	197	208	197	210
Number (95% Confidence Interval) Units: Percentages of subjects				
Day 22 (baseline)	3 (1 to 7)	5 (2 to 9)	16 (11 to 22)	23 (18 to 30)
Day 43 (N= 197,206,196,208)	11 (7 to 16)	15 (10 to 20)	30 (24 to 37)	32 (26 to 39)
Day 64 (N= 197,207,197,209)	23 (18 to 30)	25 (19 to 32)	59 (52 to 66)	48 (41 to 55)

13. Secondary Outcome

Title:	Percentages of Subjects Achieving Seroconversion or Significant Increase in Antibody Titers, After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Heterologous A/Turkey/Turkey/1/2005 Strain.
▼ Description:	To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine aH5N1, each containing 7.5µg of H5N1 antigen, against the heterologous A/turkey/Turkey/1/2005 strain, in terms of percentages of subjects achieving seroconversion or significant increase in antibody titer as measured by HI and SRH assays.
Time Frame:	Day 43/Day 22 and Day 64/Day 22)
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description
The analysis was performed on FAS population.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs) HI Titers	TIV + aH5N1 (>60 Yrs) HI Titers	TIV + aH5N1 (18-60 Yrs) SRH Areas	TIV + aH5N1 (>60 Yrs) SRH Areas
▼ Arm/Group Description:	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).

Number of Participants Analyzed	197	207	197	209
Number (95% Confidence Interval) Units: Percentages of subjects				
Day 43/Day 22 (N= 197,206,196,207,196,208)	9 (5 to 13)	8 (5 to 12)	18 (13 to 24)	10 (6 to 14)
Day 64/Day 22	19 (14 to 25)	19 (14 to 25)	49 (42 to 56)	32 (26 to 39)

14. Secondary Outcome

Title:	Percentages of Subjects With MN Titers ≥20, ≥40, ≥80, After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Homologous A/Vietnam/1194/2004 Strain.
▼ Description:	To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine (aH5N1), each containing 7.5µg of H5N1 antigen, against the homologous A/Vietnam/1194/2004 strain, in terms of percentages of subjects achieving MN Titers ≥20, ≥ 40, ≥80 on Days 22, Day 43 and Day 64.
Time Frame:	Day 22, Day 43 and Day 64
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description
The analysis was performed on FAS population.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs)	TIV + aH5N1 (>60 Yrs)
▼ Arm/Group Description:	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 influenza vaccine (aH5N1).
Number of Participants Analyzed	197	209
Number (95% Confidence Interval) Units: Percentages of subjects		
Day 22 (MN titer ≥ 20)	3 (1 to 6)	2 (1 to 5)

Day 43 (MN titer ≥ 20; N= 197,50,207,53)	27 (21 to 34)	25 (19 to 31)
Day 64 (MN titer ≥ 20; N= 197,49,208,52)	79 (73 to 85)	72 (65 to 78)
Day 22 (MN titer ≥ 40)	2 (0 to 4)	1 (0 to 3)
Day 43 (MN titer ≥ 40; N= 197,50,207,53)	16 (11 to 22)	19 (14 to 25)
Day 64 (MN titer ≥ 40; N= 197,49,208,52)	67 (60 to 74)	57 (50 to 64)
Day 22 (MN titer ≥ 80)	1 (0 to 4)	0 (0 to 2)
Day 43 (MN titer ≥ 80; N= 197,50,207,53)	9 (6 to 14)	13 (8 to 18)
Day 64 (MN titer ≥ 80; N= 197,49,208,52)	50 (43 to 57)	33 (26 to 40)

15. Secondary Outcome

Title:	Percentages of Subjects With MN Titers ≥20, ≥40, ≥80, After Two Doses of the Adjuvanted Pandemic aH5N1 Vaccine Against the Heterologous A/Turkey/Turkey/1/2005 Strain.
▼ Description:	To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine aH5N1, each containing 7.5µg of H5N1 antigen, against the heterologous A/turkey/Turkey/1/2005 Strain, in terms of percentages of subjects achieving MN Titers ≥20, ≥ 40, ≥80 on Day 22, Day 43 and Day 64.
Time Frame:	Day 22, Day 43 and Day 64
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

The analysis was performed on FAS population.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs)	TIV + aH5N1 (>60 Yrs)
▼ Arm/Group Description:	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of

		adjuvanted pandemic H5N1 influenza vaccine (aH5N1).
Number of Participants Analyzed	197	210
Number (95% Confidence Interval) Units: Percentages of subjects		
Day 22 (MN titer≥20)	5 (2 to 8)	9 (6 to 14)
Day 43 (MN titer ≥ 20; N= 196,50,207,53)	23 (17 to 29)	21 (15 to 27)
Day 64 (MN titer ≥ 20; N= 197,49,208,52)	59 (52 to 66)	47 (40 to 54)
Day 22 (MN titer ≥ 40)	3 (1 to 7)	3 (1 to 7)
Day 43 (MN titer ≥ 40; N= 196,50,208,53)	13 (8 to 18)	14 (9 to 19)
Day 64 (MN titer ≥ 40; N= 197,49,208,52)	39 (32 to 46)	30 (24 to 37)
Day 22 (MN titer ≥ 80)	2 (1 to 5)	0.012 (0.012 to 3)
Day 43 (MN titer ≥ 80; N= 196,50,207,53)	8 (4 to 12)	6 (3 to 10)
Day 64 (MN titer ≥ 80; N= 197,49,208,52)	19 (14 to 26)	12 (8 to 17)

16. Secondary Outcome

Title:	Percentages of Subjects Achieving at Least a Four-fold Rise in MN Antibody Titer on Day 43 and Day 64, Compared to Day 22 Against Homologous Strains.
▼ Description:	To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine aH5N1, each containing 7.5µg of H5N1 antigen, against the homologous A/Vietnam/1194/2004 strain, in terms of percentages of subjects achieving at least a four-fold rise in MN antibody titer on Day 43 and Day 64, compared to Day 22.
Time Frame:	Day 43/Day 22 and Day 64/Day 22
Safety Issue?	No

▼ Outcome Measure Data ✔

▼ Analysis Population Description
The analysis was performed on FAS population.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs)	TIV + aH5N1 (>60 Yrs)
▼ Arm/Group Description:	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of non adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 influenza vaccine (aH5N1).
Number of Participants Analyzed	197	208
Number (95% Confidence Interval) Units: Percentages of subjects		
Day 43/Day 22 (N= 197,50,207,53)	14 (10 to 20)	18 (13 to 24)
Day 64/Day 22 (N= 197,49,208,52)	65 (58 to 72)	55 (48 to 62)

17. Secondary Outcome

Title:	Percentages of Subjects Achieving at Least a Four-fold Rise in MN Antibody Titer on Day 43 and Day 64, Compared to Day 22 Against Heterologous Strains.
▼ Description:	To evaluate the immunogenicity of two doses of the adjuvanted pandemic vaccine (aH5N1), each containing 7.5µg of H5N1 antigen, against Heterologous A/turkey/Turkey/1/2005 Strain, in terms of percentages of subjects achieving at least a four-fold rise in MN antibody titer on Day 43 and Day 64, compared to Day 22.
Time Frame:	Day 43/Day 22 and Day 64/Day 22
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description
The analysis was performed on FAS population.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs)	TIV + aH5N1 (>60 Yrs)

▼ Arm/Group Description:	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1)	First dose of non adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 influenza vaccine (aH5N1).
Number of Participants Analyzed	197	208
Number (95% Confidence Interval) Units: Percentages of subjects		
Day 43/Day 22 (N= 196,50,207,53)	9 (5 to 14)	9 (6 to 14)
Day 64/Day 22 (N= 197,49,208,52)	36 (29 to 43)	25 (19 to 31)

18. Secondary Outcome

Title:	Number of Subjects Reporting Unsolicited AEs After Vaccination.
▼ Description:	The number of subjects reporting any unsolicited AEs any, Possibly/probably related AEs, serious adverse events (SAEs), AEs leading to withdrawal (WD), AEs leading to death from Day 1 through Day 224 post vaccination.
Time Frame:	Day 1 through Day 224 post vaccination
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Analysis was done on safety population.

Arm/Group Title	TIV + aH5N1 (18-60 Yrs)	PL + aTIV (18-60 Yrs)	TIV + aH5N1 (>60 Yrs)	PL + aTIV (>60 Yrs)
▼ Arm/Group Description:	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of	First dose of placebo (PL) followed by two doses of adjuvanted seasonal trivalent influenza vaccine (aTIV).	First dose of non adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic	First dose of placebo (PL) followed by two doses of adjuvanted seasonal trivalent influenza vaccine (aTIV).

	adjuvanted pandemic H5N1 vaccine (aH5N1).		H5N1 influenza vaccine (aH5N1).	
Number of Participants Analyzed	2611	658	214	54
Measure Type: Number Units: Subjects				
Any AEs	1329	335	103	29
SAEs	45	10	4	3
At least possibly related AEs	357	103	25	13
AEs Leading to Premature Withdrawal	4	4	2	1
Deaths	0	0	1	0

Adverse Events

Time Frame	Throughout the study ie. Day 1 to Day 224			
Additional Description	The number of subjects in the module for Adverse Events (AEs) differs from the number of subjects in the Participant Flow module. This is because the analysis for the AEs module is based on the safety population whereas the Participant Flow module refers to the enrolled population.			
Source Vocabulary Name	MedDRA			
Assessment Type	Non-systematic Assessment			
Arm/Group Title	TIV + aH5N1 (18-60 Yrs)	PL + aTIV (18-60 Yrs)	TIV + aH5N1 (>60 Yrs)	PL + aTIV (>60 Yrs)
Arm/Group Description	First dose of non-adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1 vaccine (aH5N1).	First dose of placebo (PL) followed by two doses of adjuvanted seasonal trivalent influenza vaccine (aTIV).	First dose of non adjuvanted seasonal trivalent influenza vaccine (TIV) followed by two doses of adjuvanted pandemic H5N1	First dose of placebo (PL) followed by two doses of adjuvanted seasonal trivalent influenza vaccine (aTIV).

					influenza vaccine (aH5N1).			

Serious Adverse Events

	TIV + aH5N1 (18-60 Yrs)		PL + aTIV (18-60 Yrs)		TIV + aH5N1 (>60 Yrs)		PL + aTIV (>60 Yrs)	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	40/2680 (1.49%)		9/676 (1.33%)		1/222 (0.45%)		2/56 (3.57%)	
Ear and labyrinth disorders								
Sudden hearing loss * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Vertigo * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Endocrine disorders								
Goitre * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Gastrointestinal disorders								
Abdominal pain lower * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Ileus * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Inguinal hernia * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Intestinal obstruction * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Pancreatitis acute * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Hepatobiliary disorders								
Cholecystitis acute * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Cholelithiasis * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Immune system disorders								
Anaphylactic reaction * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Anaphylactic shock * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Infections and infestations								

Appendicitis [*A]	5/2680 (0.19%)	5	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Bacterial infection [*A]	0/2680 (0%)	0	1/676 (0.15%)	1	0/222 (0%)	0	0/56 (0%)	0
Endometritis [*A]	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Gastroenteritis [*A]	2/2680 (0.07%)	2	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Gastroenteritis clostridial [*A]	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Herpes zoster opthalmic [*A]	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Influenza [*A]	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Peritonitis [*A]	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Pneumonia [*A]	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	1/56 (1.79%)	1
Pyelonephritis acute [*A]	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Viral infection [*A]	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Injury, poisoning and procedural complications								
Clavicle fracture [*A]	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Concussion [*A]	2/2680 (0.07%)	2	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Foot fracture [*A]	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Gas poisoning [*A]	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Humerus fracture [*A]	0/2680 (0%)	0	0/676 (0%)	0	0/222 (0%)	0	1/56 (1.79%)	1
Ligament rupture [*A]	0/2680 (0%)	0	1/676 (0.15%)	1	0/222 (0%)	0	0/56 (0%)	0
Ligament sprain [*A]	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Skull fracture [*A]	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Thermal burn [*A]	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Vaccination failure [*A]	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Musculoskeletal and connective tissue disorders								
Back pain [*A]	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Bone cyst [*A]	0/2680 (0%)	0	1/676 (0.15%)	1	0/222 (0%)	0	0/56 (0%)	0
Intervertebral disc protrusion [*A]	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)								
Breast cancer * A	1/2680 (0.04%)	1	1/676 (0.15%)	1	0/222 (0%)	0	0/56 (0%)	0
Cerebellar haemangioma * A	0/2680 (0%)	0	1/676 (0.15%)	1	0/222 (0%)	0	0/56 (0%)	0
Malignant melanoma * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Pancreatic neoplasm * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Rectal cancer * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Uterine leiomyoma * A	2/2680 (0.07%)	2	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Nervous system disorders								
Cerebral infraction * A	0/2680 (0%)	0	1/676 (0.15%)	1	0/222 (0%)	0	1/56 (1.79%)	1
Dystonia * A	0/2680 (0%)	0	1/676 (0.15%)	1	0/222 (0%)	0	0/56 (0%)	0
Subarachnoid haemorrhage * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Pregnancy, puerperium and perinatal conditions								
Imminent abortion * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Psychiatric disorders								
Anxiety disorder * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Schizophrenia,paranoid type * A	0/2680 (0%)	0	1/676 (0.15%)	1	0/222 (0%)	0	0/56 (0%)	0
Renal and urinary disorders								
Urethral caruncle * A	0/2680 (0%)	0	1/676 (0.15%)	1	0/222 (0%)	0	0/56 (0%)	0
Reproductive system and breast disorders								
Ovarian cyst * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0

Respiratory, thoracic and mediastinal disorders								
Bronchial hyperactivity * A	0/2680 (0%)	0	0/676 (0%)	0	0/222 (0%)	0	1/56 (1.79%)	1
Pneumothorax * A	1/2680 (0.04%)	1	0/676 (0%)	0	0/222 (0%)	0	0/56 (0%)	0
Surgical and medical procedures								
Haemorrhoid operation * A	0/2680 (0%)	0	0/676 (0%)	0	1/222 (0.45%)	1	0/56 (0%)	0

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA

▼ Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	5%							
	TIV + aH5N1 (18-60 Yrs)		**PL + aTIV (18-60 Yrs)**		**TIV + aH5N1 (>60 Yrs)**		**PL + aTIV (>60 Yrs)**	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	2301/2680 (85.86%)		590/676 (87.28%)		176/222 (79.28%)		45/56 (80.36%)	
Gastrointestinal disorders								
Nausea † A	334/2680 (12.46%)	334	88/676 (13.02%)	88	19/222 (8.56%)	19	4/56 (7.14%)	4
General disorders								
Chills † A	532/2680 (19.85%)	532	152/676 (22.49%)	152	40/222 (18.02%)	40	13/56 (23.21%)	13
Fatigue † A	927/2680 (34.59%)	927	247/676 (36.54%)	247	38/222 (17.12%)	38	9/56 (16.07%)	9
Injection site erythema † A	1041/2680 (38.84%)	1041	248/676 (36.69%)	248	87/222 (39.19%)	87	18/56 (32.14%)	18
Injection site haemorrahage * A	367/2680 (13.69%)	367	111/676 (16.42%)	111	33/222 (14.86%)	33	13/56 (23.21%)	13
Injection site induration † A	830/2680 (30.97%)	830	195/676 (28.85%)	195	42/222 (18.92%)	42	13/56 (23.21%)	13

Injection site pain †A	1738/2680 (64.85%)	1738	459/676 (67.9%)	459	96/222 (43.24%)	96	21/56 (37.5%)	21
Injection site swelling †A	632/2680 (23.58%)	632	177/676 (26.18%)	177	28/222 (12.61%)	28	6/56 (10.71%)	6
Malaise †A	542/2680 (20.22%)	542	161/676 (23.82%)	161	33/222 (14.86%)	33	7/56 (12.5%)	7
Infections and infestations								
Nasopharyngitis *A	216/2680 (8.06%)	216	59/676 (8.73%)	59	7/222 (3.15%)	7	0/56 (0%)	0
Rhinitis *A	83/2680 (3.1%)	83	27/676 (3.99%)	27	4/222 (1.8%)	4	3/56 (5.36%)	3
Upper respiratory tract infection *A	176/2680 (6.57%)	176	44/676 (6.51%)	44	8/222 (3.6%)	8	5/56 (8.93%)	5
Musculoskeletal and connective tissue disorders								
Arthralgia †A	306/2680 (11.42%)	306	97/676 (14.35%)	97	19/222 (8.56%)	19	6/56 (10.71%)	6
Myalgia †A	1088/2680 (40.6%)	1088	296/676 (43.79%)	296	69/222 (31.08%)	69	17/56 (30.36%)	17
Nervous system disorders								
Headache †A	1031/2680 (38.47%)	1031	253/676 (37.43%)	253	54/222 (24.32%)	54	18/56 (32.14%)	18
Skin and subcutaneous tissue disorders								
Hyperhidrosis †A	356/2680 (13.28%)	356	84/676 (12.43%)	84	14/222 (6.31%)	14	6/56 (10.71%)	6

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA

Limitations and Caveats

None

More Information

Certain Agreements

Principal Investigators are NOT employed by the organization sponsoring the study.

The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is less than or equal to 60 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

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