Clinical trial results:
A Phase III Stratified, Randomized, Controlled, Observer-Blind, Multicenter Study to Evaluate the Safety, Tolerability, and Immunogenicity of Two Doses of aH5N1 when Administered to Adult and Elderly Subjects With and Without Immunosuppressive Conditions.

Summary

EudraCT number	2011-003573-28
Trial protocol	IT
Global end of trial date	04 May 2015

Results information

Result version number	v1 (current)
This version publication date	10 October 2018
First version publication date	10 October 2018

Trial information

Trial identification

Sponsor protocol code	V87_26

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02107807
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Seqirus
Sponsor organisation address	The Point, 29 Market Street, Maidenhead, United Kingdom,
Public contact	Clinical Trial Disclosure Manager, Seqirus, seqirus.clinicaltrials@seqirus.com
Scientific contact	Clinical Trial Disclosure Manager, Seqirus, seqirus.clinicaltrials@seqirus.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 October 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 May 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Immunogenicity Objective
To evaluate homologous antibody responses to aH5N1 vaccine 3 weeks after second vaccination (day 43) according to CHMP immunogenicity criteria in adult (18 through 60 years of age) and elderly (≥61 years of age) subjects who are healthy or with immunosuppressive conditions, as measured by hemagglutination inhibition (HI) assay

Primary Safety Objective
To evaluate in pooled age groups 18 years of age and older solicited and unsolicited adverse events in adults and elderly subjects who are healthy or with immunosuppressive conditions who have received aTIV or aH5N1 vaccine

Protection of trial subjects:

This clinical study was designed, implemented and reported in accordance with the International Conference on Harmonisation (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations (including European Directive 2001/20/EC and US CFR Title 21), the Sponsor's codes on protection of human rights, and with the ethical principles laid down in the Declaration of Helsinki (European Council 2001, US Code of Federal Regulations 1997, ICH 1997, Declaration of Helsinki).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 April 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 108
Country: Number of subjects enrolled	Italy: 289
Country: Number of subjects enrolled	Australia: 142
Worldwide total number of subjects	539
EEA total number of subjects	397

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	373
From 65 to 84 years	162
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled from 15 sites in 3 countries: Australia (3 sites), Germany (4 sites), Italy (8 sites)

Pre-assignment

Screening details:

All enrolled subjects were included in the trial

Period 1

Period 1 title	Overall Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

This is an observer-blind study. All vaccines were administered only by unblinded personnel who were qualified to perform that function under applicable local laws and regulations for the specific study site.

Arms

Are arms mutually exclusive?	Yes
Arm title	aH5N1, ≥ 18 to ≤ 60 years/with immunosuppressive conditions

Arm description:

Subjects ≥ 18 to ≤ 60 years of age with underlying immunosuppressive who provided immunogenicity data at Day 1 and Day 43

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

FAS for secondary (SRH) objective: All subjects in the All Enrolled Set who are randomized, received at least one study vaccination and provided immunogenicity data (SRH assay, homologous strain) at baseline (Day 1), 3 weeks after first vaccination (Day 22) and 3 weeks after (planned) second vaccination (Day 43) – FAS Secondary SRH.

Arm type	Experimental
Investigational medicinal product name	Monovalent MF59-adjuvanted A/H5N1 influenza vaccine (aH5N1)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 IM injections administered 3 weeks apart to the deltoid muscle.

Arm title	aTIV, ≥ 18 to ≤ 60 years/with immunosuppressive conditions

Arm description:

Subjects ≥ 18 to ≤ 60 years of age with immunosuppressive conditions who provided immunogenicity data at Day 1 and Day 43

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

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Arm type	Experimental

Investigational medicinal product name	Trivalent inactivated MF59-adjuvanted subunit influenza vaccine (aTIV)
Investigational medicinal product code	
Other name	Fluad
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 IM injections administered 3 weeks apart to the deltoid muscle.

Arm title	aH5N1, ≥ 18 to ≤ 60 years, healthy

Arm description:

Healthy subjects ≥ 18 to ≤ 60 years of age who provided immunogenicity data at Day 1 and Day 43

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

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Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 IM injections administered 3 weeks apart to the deltoid muscle.

Arm title	aTIV, ≥ 18 to ≤ 60 years/healthy

Arm description:

Healthy subjects ≥ 18 to ≤ 60 years of age who provided immunogenicity data at Day 1 and Day 43

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

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Other name	Fluad
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 IM injections administered 3 weeks apart to the deltoid muscle.

Arm title	aH5N1, ≥61 years/with immunosuppressive conditions

Arm description:

Subjects ≥ 61 years of age with underlying immunosuppressive conditions who provided immunogenicity data at Day 1 and Day 43

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

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Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 IM injections administered 3 weeks apart to the deltoid muscle.

Arm title	aTIV, ≥61 years/with immunosuppressive conditions

Arm description:

Subjects ≥ 61 years of age with immunosuppressive conditions who provided immunogenicity data at Day 1 and Day 43

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

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Other name	Fluad
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 IM injections administered 3 weeks apart to the deltoid muscle.

Arm title	aH5N1, ≥61 years/healthy

Arm description:

Healthy subjects ≥ 61 years of age who provided immunogenicity data at Day 1 and Day 43.

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

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Dosage and administration details:

2 IM injections administered 3 weeks apart to the deltoid muscle.

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Arm description:

Healthy subjects ≥ 61 years of age who provided immunogenicity data at Day 1 and Day 43.

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

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Investigational medicinal product name	Trivalent inactivated MF59-adjuvanted subunit influenza vaccine (aTIV)
Investigational medicinal product code	
Other name	Fluad
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 IM injections administered 3 weeks apart to the deltoid muscle.

Number of subjects in period 1	aH5N1, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aTIV, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aH5N1, ≥ 18 to ≤ 60 years, healthy
Started	149	31	58
Completed	144	29	58
Not completed	5	2	0
Adverse event, serious fatal	1	-	-
Consent withdrawn by subject	2	-	-
Adverse event, non-fatal	1	-	-
Other	-	1	-
Lost to follow-up	1	1	-

Number of subjects in period 1	aTIV, ≥ 18 to ≤ 60 years/healthy	aH5N1, ≥61 years/with immunosuppressive conditions	aTIV, ≥61 years/with immunosuppressive conditions
Started	33	148	31
Completed	31	141	29
Not completed	2	7	2
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	1	4	1
Adverse event, non-fatal	-	1	-
Other	-	-	-
Lost to follow-up	1	1	1

Number of subjects in period 1	aH5N1, ≥61 years/healthy	aTIV, ≥61 years/healthy
Started	62	27

Completed	59	25
Not completed	3	2
Adverse event, serious fatal	-	-
Consent withdrawn by subject	-	-
Adverse event, non-fatal	-	-
Other	-	-
Lost to follow-up	3	2

Baseline characteristics

Reporting groups

Reporting group title	aH5N1, ≥ 18 to ≤ 60 years/with immunosuppressive conditions

Reporting group description:

Subjects ≥ 18 to ≤ 60 years of age with underlying immunosuppressive who provided immunogenicity data at Day 1 and Day 43

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

FAS for secondary (SRH) objective: All subjects in the All Enrolled Set who are randomized, received at least one study vaccination and provided immunogenicity data (SRH assay, homologous strain) at baseline (Day 1), 3 weeks after first vaccination (Day 22) and 3 weeks after (planned) second vaccination (Day 43) – FAS Secondary SRH.

Reporting group title	aTIV, ≥ 18 to ≤ 60 years/with immunosuppressive conditions

Reporting group description:

Subjects ≥ 18 to ≤ 60 years of age with immunosuppressive conditions who provided immunogenicity data at Day 1 and Day 43

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

FAS for secondary (SRH) objective: All subjects in the All Enrolled Set who are randomized, received at least one study vaccination and provided immunogenicity data (SRH assay, homologous strain) at baseline (Day 1), 3 weeks after first vaccination (Day 22) and 3 weeks after (planned) second vaccination (Day 43) – FAS Secondary SRH.

Reporting group title	aH5N1, ≥ 18 to ≤ 60 years, healthy

Reporting group description:

Healthy subjects ≥ 18 to ≤ 60 years of age who provided immunogenicity data at Day 1 and Day 43

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

FAS for secondary (SRH) objective: All subjects in the All Enrolled Set who are randomized, received at least one study vaccination and provided immunogenicity data (SRH assay, homologous strain) at baseline (Day 1), 3 weeks after first vaccination (Day 22) and 3 weeks after (planned) second vaccination (Day 43) – FAS Secondary SRH.

Reporting group title	aTIV, ≥ 18 to ≤ 60 years/healthy

Reporting group description:

Healthy subjects ≥ 18 to ≤ 60 years of age who provided immunogenicity data at Day 1 and Day 43

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

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Reporting group title	aH5N1, ≥61 years/with immunosuppressive conditions

Reporting group description:

Subjects ≥ 61 years of age with underlying immunosuppressive conditions who provided immunogenicity data at Day 1 and Day 43

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

FAS for secondary (SRH) objective: All subjects in the All Enrolled Set who are randomized, received at

least one study vaccination and provided immunogenicity data (SRH assay, homologous strain) at baseline (Day 1), 3 weeks after first vaccination (Day 22) and 3 weeks after (planned) second vaccination (Day 43) – FAS Secondary SRH.

Reporting group title	aTIV, ≥61 years/with immunosuppressive conditions

Reporting group description:

Subjects ≥ 61 years of age with immunosuppressive conditions who provided immunogenicity data at Day 1 and Day 43

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

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Reporting group title	aH5N1, ≥61 years/healthy

Reporting group description:

Healthy subjects ≥ 61 years of age who provided immunogenicity data at Day 1 and Day 43.

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

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Reporting group title	aTIV, ≥61 years/healthy

Reporting group description:

Healthy subjects ≥ 61 years of age who provided immunogenicity data at Day 1 and Day 43.

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

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Reporting group values	aH5N1, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aTIV, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aH5N1, ≥ 18 to ≤ 60 years, healthy
Number of subjects	149	31	58
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	149	31	58
From 65-84 years	0	0	0
85 years and over	0	0	0

Age continuous Units: years			
arithmetic mean	46.2	44.5	37.9
standard deviation	± 8.85	± 8.26	± 12.87
Gender categorical Units: Subjects			
Female	22	7	36
Male	127	24	22
Race Units: Subjects			
Asian	3	1	0
Black	6	3	1
Native Pacific Islander	2	0	0
White	136	27	57
Other	2	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	9	4	2
Not Hispanic or Latino	140	27	56
Not reported	0	0	0
Unknown	0	0	0
Weight Units: kilogram(s)			
arithmetic mean	77.2	75.9	70.2
standard deviation	± 15.68	± 11.86	± 15.50
BMI Units: kilogram(s)/square meter			
arithmetic mean	25.0	25.2	24.6
standard deviation	± 4.09	± 4.09	± 5.31

Reporting group values	aTIV, ≥ 18 to ≤ 60 years/healthy	aH5N1, ≥61 years/with immunosuppressive conditions	aTIV, ≥61 years/with immunosuppressive conditions
Number of subjects	33	148	31
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	33	64	10
From 65-84 years	0	84	20
85 years and over	0	0	1
Age continuous Units: years			
arithmetic mean	38.1	66.2	67.4
standard deviation	± 13.31	± 4.74	± 5.37

Gender categorical Units: Subjects			
Female	15	13	3
Male	18	135	28
Race Units: Subjects			
Asian	0	1	0
Black	1	1	1
Native Pacific Islander	0	0	0
White	32	142	30
Other	0	4	0
Ethnicity Units: Subjects			
Hispanic or Latino	0	4	0
Not Hispanic or Latino	33	144	31
Not reported	0	0	0
Unknown	0	0	0
Weight Units: kilogram(s)			
arithmetic mean	79.6	78.1	77.9
standard deviation	± 19.89	± 13.58	± 12.84
BMI Units: kilogram(s)/square meter			
arithmetic mean	26.2	26.3	26.0
standard deviation	± 5.41	± 4.28	± 4.03

Reporting group values	aH5N1, ≥61 years/healthy	aTIV, ≥61 years/healthy	Total
Number of subjects	62	27	539
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	18	10	373
From 65-84 years	42	16	162
85 years and over	2	1	4
Age continuous Units: years			
arithmetic mean	69.6	68.6	
standard deviation	± 7.04	± 7.02	-
Gender categorical Units: Subjects			
Female	29	16	141
Male	33	11	398

Race Units: Subjects			
Asian	0	0	5
Black	0	0	13
Native Pacific Islander	0	0	2
White	62	27	513
Other	0	0	6
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	19
Not Hispanic or Latino	59	26	516
Not reported	3	1	4
Unknown	0	0	0
Weight Units: kilogram(s)			
arithmetic mean	79.8	81.6	
standard deviation	± 18.10	± 18.18	-
BMI Units: kilogram(s)/square meter			
arithmetic mean	27.6	29.3	
standard deviation	± 5.51	± 7.40	-

End points

End points reporting groups

Reporting group title	aH5N1, ≥ 18 to ≤ 60 years/with immunosuppressive conditions

Reporting group description:

Subjects ≥ 18 to ≤ 60 years of age with underlying immunosuppressive who provided immunogenicity data at Day 1 and Day 43

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

FAS for secondary (SRH) objective: All subjects in the All Enrolled Set who are randomized, received at least one study vaccination and provided immunogenicity data (SRH assay, homologous strain) at baseline (Day 1), 3 weeks after first vaccination (Day 22) and 3 weeks after (planned) second vaccination (Day 43) – FAS Secondary SRH.

Reporting group title	aTIV, ≥ 18 to ≤ 60 years/with immunosuppressive conditions

Reporting group description:

Subjects ≥ 18 to ≤ 60 years of age with immunosuppressive conditions who provided immunogenicity data at Day 1 and Day 43

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

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Reporting group title	aH5N1, ≥ 18 to ≤ 60 years, healthy

Reporting group description:

Healthy subjects ≥ 18 to ≤ 60 years of age who provided immunogenicity data at Day 1 and Day 43

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

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Reporting group title	aTIV, ≥ 18 to ≤ 60 years/healthy

Reporting group description:

Healthy subjects ≥ 18 to ≤ 60 years of age who provided immunogenicity data at Day 1 and Day 43

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

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Reporting group title	aH5N1, ≥61 years/with immunosuppressive conditions

Reporting group description:

Subjects ≥ 61 years of age with underlying immunosuppressive conditions who provided immunogenicity data at Day 1 and Day 43

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

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Reporting group title	aTIV, ≥61 years/with immunosuppressive conditions

Reporting group description:

Subjects ≥ 61 years of age with immunosuppressive conditions who provided immunogenicity data at Day 1 and Day 43

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

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Reporting group description:

Healthy subjects ≥ 61 years of age who provided immunogenicity data at Day 1 and Day 43.

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Healthy subjects ≥ 61 years of age who provided immunogenicity data at Day 1 and Day 43.

FAS for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay, homologous strain) at baseline (Day 1) and 3 weeks after (planned) second vaccination (Day 43).

FAS for secondary (SRH) objective: All subjects in the All Enrolled Set who are randomized, received at least one study vaccination and provided immunogenicity data (SRH assay, homologous strain) at baseline (Day 1), 3 weeks after first vaccination (Day 22) and 3 weeks after (planned) second vaccination (Day 43) – FAS Secondary SRH.

Subject analysis set title	aH5N1, ≥18 years of age
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed set who were in the solicited safety set and/or in the unsolicited safety set who received aH5N1.

Subject analysis set title	aTIV, ≥18 years of age
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed set who were in the solicited safety set and/or in the unsolicited safety set who received aH5N1.

Primary: Immunogenicity Endpoint: Geometric Mean Ratios (Day 43/Day 1), as determined by HI assay

End point title	Immunogenicity Endpoint: Geometric Mean Ratios (Day 43/Day 1), as determined by HI assay[1]

End point description:

Geometric Mean ratios (GMRs) on Day 43 versus Day 1 (baseline) in adult (18 through 60 years of age) and elderly (≥61 years of age) 3 weeks after the second vaccination (Day 43) according to CHMP immunogenicity criteria in subjects who are healthy or with immunosuppressive conditions as determined by Hemagglutination Inhibition (HI) assay.

Full Analysis Set (FAS) for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay) at baseline (Day

1) and 3 weeks after the (planned) second vaccination (Day 43).

End point type	Primary

End point timeframe:

Day 43: Day 1

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Analyses for this endpoint were performed with descriptive statistics

End point values	aH5N1, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aTIV, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aH5N1, ≥ 18 to ≤ 60 years, healthy	aTIV, ≥ 18 to ≤ 60 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	146[2]	31[3]	58[4]	33[5]
Units: titer ratios				
geometric mean (confidence interval 95%)	2.01 (1.69 to 2.39)	1.09 (0.75 to 1.59)	3.61 (2.67 to 4.89)	1.09 (0.73 to 1.63)

Notes:

[2] - N for Day 43 = 143

[3] - N for Day 43 = 30

[4] - N for Day 43 = 57

[5] - N for Day 43 = 32

End point values	aH5N1, ≥61 years/with immunosuppressive conditions	aTIV, ≥61 years/with immunosuppressive conditions	aH5N1, ≥61 years/healthy	aTIV, ≥61 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	147[6]	31[7]	62	26
Units: titer ratios				
geometric mean (confidence interval 95%)	2.40 (1.98 to 2.92)	1.37 (0.90 to 2.08)	2.94 (2.16 to 4.01)	1.05 (0.65 to 1.71)

Notes:

[6] - N for Day 43 = 139

[7] - N for Day 43 = 30

Statistical analyses

No statistical analyses for this end point

Primary: Immunogenicity Endpoint: Percentage of subjects achieving seroconversion on Day 43 as determined by HI assay

End point title	Immunogenicity Endpoint: Percentage of subjects achieving seroconversion on Day 43 as determined by HI assay[8]

End point description:

Percentage of subjects achieving seroconversion (defined as HI ≥1:40 for subjects who were seronegative at baseline [Day 1 HI titer <1:10] or a minimum 4-fold increase in HI titer for subjects who were seropositive at baseline [Day 1 HI titer ≥1:10]) on Day 43 in adult (18 through 60 years of age) and elderly (≥61 years of age) according to CHMP immunogenicity criteria in subjects who are healthy or with immunosuppressive conditions as determined by Hemagglutination Inhibition (HI) assay.

Full Analysis Set (FAS) for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay) at baseline (Day 1) and 3 weeks after the (planned) second vaccination (Day 43).

End point type	Primary

End point timeframe:

Day 43

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Analyses for this endpoint were performed with descriptive statistics

End point values	aH5N1, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aTIV, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aH5N1, ≥ 18 to ≤ 60 years, healthy	aTIV, ≥ 18 to ≤ 60 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	146[9]	31[10]	58[11]	33[12]
Units: percentage of subjects				
number (confidence interval 95%)	19.18 (13.1 to 26.5)	0 (0 to 0)	43.10 (30.2 to 56.8)	3.03 (0.08 to 15.8)

Notes:

[9] - N for Day 43 = 143

[10] - N for Day 43 = 30

[11] - N for Day 43 = 57

[12] - N for Day 43 = 32

End point values	aH5N1, ≥61 years/with immunosuppressive conditions	aTIV, ≥61 years/with immunosuppressive conditions	aH5N1, ≥61 years/healthy	aTIV, ≥61 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	147[13]	31[14]	62	26
Units: percentage of subjects				
number (confidence interval 95%)	24.49 (17.8 to 32.3)	3.23 (0.08 to 16.7)	30.65 (19.6 to 43.7)	3.85 (0.1 to 19.6)

Notes:

[13] - N for Day 43 = 139

[14] - N for Day 43 = 30

Statistical analyses

No statistical analyses for this end point

Primary: Immunogenicity Endpoint: Percentage of subjects with HI titer ≥1:40 (Day 43)

End point title	Immunogenicity Endpoint: Percentage of subjects with HI titer ≥1:40 (Day 43)[15]

End point description:

Percentage of subjects with HI titer ≥1:40 on Day 43 in adult (18 through 60 years of age) and elderly (≥61 years of age) according to CHMP immunogenicity criteria in subjects who are healthy or with immunosuppressive conditions as determined by Hemagglutination Inhibition (HI) assay.

Full Analysis Set (FAS) for primary objective: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay) at baseline (Day 1) and 3 weeks after the (planned) second vaccination (Day 43).

End point type	Primary

End point timeframe:

Day 43

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Analyses for this endpoint were performed with descriptive statistics

End point values	aH5N1, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aTIV, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aH5N1, ≥ 18 to ≤ 60 years, healthy	aTIV, ≥ 18 to ≤ 60 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	146[16]	31[17]	58[18]	33[19]
Units: percentage of subjects				
number (confidence interval 95%)	20 (14 to 27.8)	0 (0 to 0)	46 (32.4 to 59.3)	3 (0.08 to 16.2)

Notes:

[16] - N for Day 43 = 143

[17] - N for Day 43 = 30

[18] - N for Day 43 = 57

[19] - N for Day 43 = 32

End point values	aH5N1, ≥61 years/with immunosuppressive conditions	aTIV, ≥61 years/with immunosuppressive conditions	aH5N1, ≥61 years/healthy	aTIV, ≥61 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	147[20]	31[21]	62	26
Units: percentage of subjects				
number (confidence interval 95%)	27 (20.1 to 35.5)	7 (0.8 to 22.1)	32 (20.9 to 45.3)	4 (0.1 to 19.6)

Notes:

[20] - N for Day 43 = 139

[21] - N for Day 43 = 30

Statistical analyses

No statistical analyses for this end point

Primary: Safety Endpoint: Percentage of subjects with solicited local, solicited systemic, and other AEs

End point title	Safety Endpoint: Percentage of subjects with solicited local, solicited systemic, and other AEs[22]

End point description:

Percentage of subjects with solicited AEs that occur within 7 days following each vaccination

Solicited Safety Set: All subjects in the Exposed Set with any solicited AE data and/or indicators of solicited AEs (ie, use of analgesics/antipyretics).

End point type	Primary

End point timeframe:

Day 1 through Day 7

Notes:

[22] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Analyses for this endpoint were performed with descriptive statistics

End point values	aH5N1, ≥18 years of age	aTIV, ≥18 years of age		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	415	122		
Units: percentage of subjects				
number (not applicable)				
Solicited AEs, Any	75.9	73.8		
Solicited Local AEs	68.7	68.0		
Solicited Systemic AEs	53.5	53.3		
Other	5.8	6.6		

Statistical analyses

No statistical analyses for this end point

Primary: Safety Endpoint: Percentage of subjects with unsolicited AEs reported

End point title	Safety Endpoint: Percentage of subjects with unsolicited AEs reported[23]

End point description:

Percentage of subjects with any unsolicited AEs reported within 21 days after each vaccination within each vaccine group.

Unsolicited Safety Set: All subjects in the Exposed Set with unsolicited AE data.

End point type	Primary

End point timeframe:

Day 1 through Day 21

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Analyses for this endpoint were performed with descriptive statistics

End point values	aH5N1, ≥18 years of age	aTIV, ≥18 years of age		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	413	122		
Units: Percentage of subjects				
number (not applicable)				
Unsolicited AEs, Any	42.4	33.6		
Unsolicited AEs, Mild	17.7	11.5		
Unsolicited AEs, Moderate	19.4	17.2		
Unsolicited AEs, Severe	5.3	4.9		
Unsolicited AEs, Related	10.4	7.4		

Statistical analyses

No statistical analyses for this end point

Primary: Safety Endpoint: Percentage of subjects with SAEs, NOCDs, medically attended AEs, AESIs, AEs leading to withdrawal from the study

End point title	Safety Endpoint: Percentage of subjects with SAEs, NOCDs, medically attended AEs, AESIs, AEs leading to withdrawal from the study[24]

End point description:

Percentage of subjects reporting SAEs, NOCDs, medically attended AEs, AESIs, AEs leading to withdrawal from the study as collected from Day 1 through Day 202.

Unsolicited Safety Set: All subjects in the Exposed Set with unsolicited AE data.

End point type	Primary

End point timeframe:

Day 1 through Day 202

Notes:

[24] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Analyses for this endpoint were performed with descriptive statistics

End point values	aH5N1, ≥18 years of age	aTIV, ≥18 years of age		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	415[25]	122		
Units: Percentage of subjects				
number (not applicable)				
Serious Adverse Events (SAE)	3.4	4.1		
Related SAEs	0.2	0		
Medically attended AEs	37.4	28.7		
AESIs	0	0		
NOCDs	3.1	0.8		
AEs leading to withdrawal	1.0	0		
AEs leading to death	0.5	0		

Notes:

[25] - N for SAEs, related SAEs, AEs leading to withdrawal and AEs leading to death = 413

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity Endpoint: Geometric Mean Ratios: Day 22/Day 1 and Day 43/Day 1 as determined by SRH

End point title	Immunogenicity Endpoint: Geometric Mean Ratios: Day 22/Day 1 and Day 43/Day 1 as determined by SRH

End point description:

Geometric Mean ratios (GMRs) for Day 22/Day 1 and Day 43/Day 1 as determined by single radial hemolysis (SRH) in adult (18 through 60 years of age) and elderly (≥61 years of age) according to CHMP immunogenicity criteria in subjects who are healthy or with immunosuppressive conditions.

FAS for Secondary Objective. SRH - All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (SRH assay) at baseline (Day 1), 3 weeks after the first vaccination (Day 22) and 3 weeks after the (planned) second vaccination (Day 43).

End point type	Secondary

End point timeframe:

Day 22/Day 1 and Day 43/Day 1

End point values	aH5N1, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aTIV, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aH5N1, ≥ 18 to ≤ 60 years, healthy	aTIV, ≥ 18 to ≤ 60 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	146[26]	31[27]	58[28]	33[29]
Units: titer ratios				
geometric mean (confidence interval 95%)				
Day 22/Day 1 - SRH	1.65 (1.43 to 1.90)	1.44 (1.05 to 1.97)	2.71 (2.19 to 3.36)	1.27 (0.95 to 1.69)
Day 43/Day 1 - SRH	3.16 (2.69 to 3.73)	1.86 (1.30 to 2.66)	7.10 (5.85 to 8.62)	1.49 (1.15 to 1.93)

Notes:

[26] - N for Day 22 = 144
N for Day 43 = 143
[27] - N for Day 22 = 30
N for Day 43 = 30
[28] - N for Day 43 = 57
[29] - N for Day 22 = 32
N for Day 43 = 32

End point values	aH5N1, ≥61 years/with immunosuppressive conditions	aTIV, ≥61 years/with immunosuppressive conditions	aH5N1, ≥61 years/healthy	aTIV, ≥61 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	147[30]	31[31]	62	26
Units: titer ratios				
geometric mean (confidence interval 95%)				
Day 22/Day 1 - SRH	1.76 (1.52 to 2.03)	1.41 (1.03 to 1.93)	1.69 (1.38 to 2.06)	1.29 (0.95 to 1.77)
Day 43/Day 1 - SRH	3.15 (2.70 to 3.68)	1.49 (1.07 to 2.08)	2.83 (2.24 to 3.58)	1.24 (0.86 to 1.79)

Notes:

[30] - N for Day 22 = 142
N for Day 43 = 139
[31] - N for Day 22 = 30
N for Day 43 = 30

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity Endpoint: Percentage of subject achieving seroconversion on Day 22 and Day 43 as determined by SRH assay

End point title	Immunogenicity Endpoint: Percentage of subject achieving seroconversion on Day 22 and Day 43 as determined by SRH assay

End point description:

Percentage of subjects achieving seroconversion on Day 22 and Day 43 in adult (18 through 60 years of age) and elderly (≥61 years of age) according to CHMP immunogenicity criteria in subjects who are healthy or with immunosuppressive conditions as determined by single radial hemolysis (SRH) assay.

FAS for Secondary Objective. SRH - All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (SRH assay) at baseline (Day 1), 3 weeks after the first vaccination (Day 22) and 3 weeks after the (planned) second vaccination (Day 43).

End point type	Secondary
End point timeframe: Day 22 and Day 43	

End point values	aH5N1, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aTIV, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aH5N1, ≥ 18 to ≤ 60 years, healthy	aTIV, ≥ 18 to ≤ 60 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	146[32]	31[33]	58[34]	33[35]
Units: percentage of subjects				
number (confidence interval 95%)				
Day 22 - SRH	33.33 (25.7 to 41.7)	30.00 (14.7 to 49.4)	63.79 (50.1 to 76)	25.00 (11.5 to 43.4)
Day 43 - SRH	61.54 (53 to 69.5)	50.00 (31.3 to 68.7)	89.47 (78.5 to 96)	37.50 (21.1 to 56.3)

Notes:

[32] - N for Day 22 = 144
N for Day 43 = 143
[33] - N for Day 22 = 30
N for Day 43 = 30
[34] - N for Day 43 = 57
[35] - N for Day 22 = 32
N for Day 43 = 32

End point values	aH5N1, ≥61 years/with immunosuppressive conditions	aTIV, ≥61 years/with immunosuppressive conditions	aH5N1, ≥61 years/healthy	aTIV, ≥61 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	147[36]	31[37]	62	23
Units: percentage of subjects				
number (confidence interval 95%)				
Day 22 - SRH	38.03 (30 to 46.5)	26.67 (12.3 to 45.9)	35.48 (23.7 to 48.7)	19.23 (6.6 to 39.4)
Day 43 - SRH	64.75 (56.2 to 72.7)	20.00 (7.7 to 38.6)	56.45 (43.3 to 69)	19.23 (6.6 to 39.4)

Notes:

[36] - N for Day 22 = 142
N for Day 43 = 139
[37] - N for Day 22 = 30
N for Day 43 = 30

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity Endpoint: Percentage of subjects with SRH area ≥25mm2 on Day 1, Day 22 and Day 43

End point title	Immunogenicity Endpoint: Percentage of subjects with SRH area ≥25mm2 on Day 1, Day 22 and Day 43

End point description:

Percentage of subjects with with SRH area ≥25mm2 on Day 1, Day 22 and Day 43 in adult (18 through

60 years of age) and elderly (≥61 years of age) according to CHMP immunogenicity criteria in subjects who are healthy or with immunosuppressive conditions as determined by single radial hemolysis (SRH) assay.

FAS for Secondary Objective. SRH - All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (SRH assay) at baseline (Day 1), 3 weeks after the first vaccination (Day 22) and 3 weeks after the (planned) second vaccination (Day 43).

End point type	Secondary
End point timeframe:	
Day 1, Day 22 and Day 43	

End point values	aH5N1, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aTIV, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aH5N1, ≥ 18 to ≤ 60 years, healthy	aTIV, ≥ 18 to ≤ 60 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	146[38]	31[39]	58[40]	33[41]
Units: percentage of subjects				
number (confidence interval 95%)				
Day 1 - SRH	13.70 (8.6 to 20.4)	6.45 (0.8 to 21.4)	5.17 (1.1 to 14.4)	3.03 (0.08 to 15.8)
Day 22 - SRH	29.86 (22.5 to 38)	23.33 (9.9 to 42.3)	34.48 (22.5 to 48.1)	12.50 (3.5 to 29)
Day 43 - SRH	60.84 (52.3 to 68.9)	30.00 (14.7 to 49.4)	87.72 (76.3 to 94.9)	21.88 (9.3 to 40)

Notes:

[38] - N for Day 22 = 144
N for Day 43 = 143
[39] - N for Day 22 = 30
N for Day 43 = 30
[40] - N for Day 43 = 57
[41] - N for Day 22 = 32
N for Day 43 = 32

End point values	aH5N1, ≥61 years/with immunosuppressive conditions	aTIV, ≥61 years/with immunosuppressive conditions	aH5N1, ≥61 years/healthy	aTIV, ≥61 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	147[42]	31[43]	62	26
Units: percentage of subjects				
number (confidence interval 95%)				
Day 1 - SRH	12.93 (8 to 19.4)	12.90 (3.6 to 29.8)	14.52 (6.9 to 25.8)	11.54 (2.4 to 30.2)
Day 22 - SRH	33.80 (26.1 to 42.2)	33.33 (17.3 to 52.8)	32.26 (20.9 to 45.3)	30.77 (14.3 to 51.8)
Day 43 - SRH	58.99 (50.3 to 67.3)	33.33 (17.3 to 52.8)	53.23 (40.1 to 66)	26.92 (11.6 to 47.8)

Notes:

[42] - N for Day 22 = 142
N for Day 43 = 139
[43] - N for Day 22 = 30
N for Day 43 = 30

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity Endpoint: Geometric Mean Ratios (Day 22/Day 1) as determined by HI assay

End point title	Immunogenicity Endpoint: Geometric Mean Ratios (Day 22/Day 1) as determined by HI assay

End point description:

Geometric Mean ratios (GMRs) on Day 22 versus Day 1 (baseline) in adult (18 through 60 years of age) and elderly (≥61 years of age) 3 weeks after the first vaccination (Day 22) according to CHMP immunogenicity criteria in subjects who are healthy or with immunosuppressive conditions as determined by Hemagglutination Inhibition (HI) assay.

FAS for Secondary Objective, HI: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay) at baseline (Day 1) and 3 weeks after the first vaccination (Day 22).

End point type	Secondary

End point timeframe:

Day 22/Day 1

End point values	aH5N1, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aTIV, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aH5N1, ≥ 18 to ≤ 60 years, healthy	aTIV, ≥ 18 to ≤ 60 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	146[44]	31[45]	58	33[46]
Units: titer ratios				
geometric mean (confidence interval 95%)	1.29 (1.14 to 1.46)	1.17 (0.89 to 1.53)	1.62 (1.30 to 2.04)	1.08 (0.79 to 1.46)

Notes:

[44] - N for Day 22 = 144

[45] - N for Day 22 = 30

[46] - N for Day 22 = 32

End point values	aH5N1, ≥61 years/with immunosuppressive conditions	aTIV, ≥61 years/with immunosuppressive conditions	aH5N1, ≥61 years/healthy	aTIV, ≥61 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	147[47]	31	62	26
Units: titer ratios				
geometric mean (confidence interval 95%)	1.47 (1.28 to 1.68)	1.03 (0.78 to 1.38)	1.73 (1.32 to 2.26)	1.14 (0.75 to 1.73)

Notes:

[47] - N for Day 22 = 142

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity Endpoint: Percentage of subjects achieving seroconversion (Day 22) as determined by HI assay

End point title	Immunogenicity Endpoint: Percentage of subjects achieving seroconversion (Day 22) as determined by HI assay

End point description:

Percentage of subjects achieving seroconversion (defined as HI ≥1:40 for subjects who were seronegative at baseline [Day 1 HI titer <1:10] or a minimum 4-fold increase in HI titer for subjects who were seropositive at baseline [Day 1 HI titer ≥1:10]) on Day 22 in adult (18 through 60 years of age) and elderly (≥61 years of age) according to CHMP immunogenicity criteria in subjects who are healthy or with immunosuppressive conditions as determined by Hemagglutination Inhibition (HI) assay.

FAS for Secondary Objective, HI: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay) at baseline (Day 1) and 3 weeks after the first vaccination (Day 22).

End point type	Secondary

End point timeframe:

Day 22

End point values	aH5N1, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aTIV, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aH5N1, ≥ 18 to ≤ 60 years, healthy	aTIV, ≥ 18 to ≤ 60 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	146[48]	31[49]	58	33[50]
Units: percentage of subjects				
number (confidence interval 95%)	4.86 (2 to 9.8)	3.33 (0.08 to 17.2)	12.07 (5 to 23.3)	3.13 (0.08 to 16.2)

Notes:

[48] - N for Day 22 = 144

[49] - N for Day 22 = 30

[50] - N for Day 22 = 32

End point values	aH5N1, ≥61 years/with immunosuppressive conditions	aTIV, ≥61 years/with immunosuppressive conditions	aH5N1, ≥61 years/healthy	aTIV, ≥61 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	147[51]	31	62	26
Units: percentage of subjects				
number (confidence interval 95%)	10.56 (6 to 16.8)	0 (0 to 0)	12.90 (5.7 to 23.9)	3.85 (0.1 to 19.6)

Notes:

[51] - N for Day 22 = 142

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity Endpoint: Percentage of subjects with HI titer ≥1:40 on Day 1 and Day 22 as determined by HI assay

End point title	Immunogenicity Endpoint: Percentage of subjects with HI titer

	≥1:40 on Day 1 and Day 22 as determined by HI assay

End point description:

Percentage of subjects with HI titer ≥1:40 on Day 22 in adult (18 through 60 years of age) and elderly (≥61 years of age) according to CHMP immunogenicity criteria in subjects who are healthy or with immunosuppressive conditions as determined by Hemagglutination Inhibition (HI) assay.

FAS for Secondary Objective, HI: All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data (HI assay) at baseline (Day 1) and 3 weeks after the first vaccination (Day 22).

End point type	Secondary

End point timeframe:

Day 1 and Day 22

End point values	aH5N1, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aTIV, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aH5N1, ≥ 18 to ≤ 60 years, healthy	aTIV, ≥ 18 to ≤ 60 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	146[52]	31[53]	58	33[54]
Units: percentage of subjects				
number (confidence interval 95%)				
Day 1 - HI	1 (0.02 to 3.8)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Day 22 - HI	6 (2.4 to 10.7)	3 (0.08 to 17.2)	12 (5 to 23.3)	3 (0.08 to 16.2)

Notes:

[52] - N for Day 22 = 144

[53] - N for Day 22 = 30

[54] - N for Day 22 = 32

End point values	aH5N1, ≥61 years/with immunosuppressive conditions	aTIV, ≥61 years/with immunosuppressive conditions	aH5N1, ≥61 years/healthy	aTIV, ≥61 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	147[55]	31	62	26
Units: percentage of subjects				
number (confidence interval 95%)				
Day 1 - HI	1 (0.02 to 3.7)	0 (0 to 0)	2 (0.04 to 8.7)	0 (0 to 0)
Day 22 - HI	11 (6 to 16.8)	0 (0 to 0)	15 (6.9 to 25.8)	4 (0.1 to 19.6)

Notes:

[55] - N for Day 22 =142

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity Endpoint: Geometric Mean Titers (HI) and Geometric Mean Area (SRH) at Day 1, Day 22 and Day 43 as determined by HI and SRH

End point title	Immunogenicity Endpoint: Geometric Mean Titers (HI) and Geometric Mean Area (SRH) at Day 1, Day 22 and Day 43 as

	determined by HI and SRH

End point description:

Geometric mean titers (HI) and Geomertric Mean Area (SRH) at the following time points: Day 1, Day 22 (3 weeks after the first vaccination), Day 43 (3 weeks after the second vaccination) in adult (18 through 60 years of age) and elderly (≥61 years of age) subjects.

FAS for Secondary Objective. SRH and HI- All subjects in the All Enrolled Set who were randomized, received at least one study vaccination and provided immunogenicity data at baseline (Day 1, SRH and HI assay), 3 weeks after the first vaccination (Day 22, SRH and HI assay) and 3 weeks after the (planned) second vaccination (Day 43, SRH assay).

End point type	Secondary

End point timeframe:

Day 1, Day 22, Day 43

End point values	aH5N1, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aTIV, ≥ 18 to ≤ 60 years/with immunosuppressive conditions	aH5N1, ≥ 18 to ≤ 60 years, healthy	aTIV, ≥ 18 to ≤ 60 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	146[56]	31[57]	58[58]	33[59]
Units: titer ratios				
geometric mean (confidence interval 95%)				
Day 1 - HI	5.14 (4.96 to 5.34)	5.00 (4.62 to 5.41)	5.09 (4.95 to 5.24)	5.00 (4.81 to 5.19)
Day 1 - SRH	8.54 (7.51 to 9.71)	8.20 (6.21 to 10.83)	7.11 (6.14 to 8.24)	6.28 (5.17 to 7.63)
Day 22 - HI	6.61 (5.83 to 7.48)	5.98 (4.55 to 7.86)	8.21 (6.55 to 10.30)	5.45 (4.02 to 7.39)
Day 22 - SRH	13.65 (11.84 to 15.74)	11.90 (8.71 to 16.26)	18.51 (14.95 to 22.92)	8.64 (6.47 to 11.52)
Day 43 - HI	10.31 (8.68 to 12.25)	5.57 (3.82 to 8.12)	18.28 (13.50 to 24.73)	5.50 (3.67 to 8.24)
Day 43 - SRH	26.50 (22.49 to 31.22)	15.58 (10.89 to 22.29)	48.58 (40.01 to 58.99)	10.17 (7.84 to 13.18)

Notes:

[56] - N for Day 22 = 144
N for Day 43 = 143

[57] - N for Day 22 = 30
N for Day 43 = 30

[58] - N for Day 43 = 57

[59] - N for Day 22 = 32
N for Day 43 = 32

End point values	aH5N1, ≥61 years/with immunosuppressive conditions	aTIV, ≥61 years/with immunosuppressive conditions	aH5N1, ≥61 years/healthy	aTIV, ≥61 years/healthy
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	147[60]	31[61]	62	26
Units: titer ratios				
geometric mean (confidence interval 95%)				
Day 1 - HI	5.37 (5.08 to 5.67)	5.29 (4.69 to 5.97)	5.44 (5.00 to 5.91)	5.00 (4.40 to 5.68)

Day 1 - SRH	8.34 (7.34 to 9.48)	10.04 (7.61 to 13.27)	8.25 (6.78 to 10.03)	8.93 (6.60 to 12.09)
Day 22 - HI	7.79 (6.81 to 8.90)	5.49 (4.12 to 7.32)	9.18 (7.02 to 12.01)	6.05 (3.99 to 9.17)
Day 22 - SRH	14.99 (12.99 to 17.30)	12.03 (8.79 to 16.46)	14.23 (11.62 to 17.42)	10.91 (7.98 to 14.91)
Day 43 - HI	12.76 (10.50 to 15.50)	7.26 (4.78 to 11.04)	15.60 (11.44 to 21.29)	5.59 (3.46 to 9.05)
Day 43 - SRH	26.85 (23.01 to 31.33)	12.71 (9.11 to 17.74)	23.91 (18.89 to 30.26)	10.48 (7.28 to 15.08)

Notes:

[60] - N for Day 22 = 142
N for Day 43 = 139
[61] - N for Day 43 = 30

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 through Day 202	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups	
Reporting group title	aH5N1, ≥ 18 years, overall safety set
Reporting group description:	
All subjects in the exposed set who were in the solicited safety set and/or in the unsolicited safety set who received aH5N1.	
Reporting group title	aTIV, ≥ 18 years, overall safety set
Reporting group description:	
All subjects in the exposed set who were in the solicited safety set and/or in the unsolicited safety set who received aTIV.	

Serious adverse events	aH5N1, ≥ 18 years, overall safety set	aTIV, ≥ 18 years, overall safety set	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 415 (3.37%)	5 / 122 (4.10%)	
number of deaths (all causes)	2	0	
number of deaths resulting from adverse events	2	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastasis to liver			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal carcinoma			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			

subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal squamous cell carcinoma			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Kidney transplant rejection			
subjects affected / exposed	0 / 415 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			

subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Road traffic accident			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 415 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			

subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal disorder			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc annular tear			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Erysipelas			

subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 415 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 415 (0.48%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Secondary syphilis			
subjects affected / exposed	0 / 415 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	0 / 415 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 415 (0.24%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	aH5N1, ≥ 18 years, overall safety set	aTIV, ≥ 18 years, overall safety set	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	312 / 415 (75.18%)	90 / 122 (73.77%)	
Nervous system disorders			
Headache			
subjects affected / exposed	91 / 415 (21.93%)	23 / 122 (18.85%)	
occurrences (all)	215	53	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	40 / 415 (9.64%)	10 / 122 (8.20%)	
occurrences (all)	93	22	
Injection site erythema			
subjects affected / exposed	82 / 415 (19.76%)	19 / 122 (15.57%)	
occurrences (all)	246	48	
Injection site haemorrhage			
subjects affected / exposed	22 / 415 (5.30%)	5 / 122 (4.10%)	
occurrences (all)	73	6	
Injection site induration			
subjects affected / exposed	74 / 415 (17.83%)	26 / 122 (21.31%)	
occurrences (all)	199	63	
Injection site pain			
subjects affected / exposed	249 / 415 (60.00%)	75 / 122 (61.48%)	
occurrences (all)	746	230	
Fatigue			
subjects affected / exposed	122 / 415 (29.40%)	37 / 122 (30.33%)	
occurrences (all)	447	138	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	52 / 415 (12.53%)	13 / 122 (10.66%)	
occurrences (all)	115	38	
Nausea			
subjects affected / exposed	44 / 415 (10.60%)	12 / 122 (9.84%)	
occurrences (all)	85	32	
Musculoskeletal and connective tissue			

disorders Arthralgia subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all)	 68 / 415 (16.39%) 204 145 / 415 (34.94%) 418	 22 / 122 (18.03%) 53 47 / 122 (38.52%) 141	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 46 / 415 (11.08%) 118	 12 / 122 (9.84%) 30	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported