



Clinical trial results:

A Phase 2/3, randomized, controlled, observer-blind, multi-center trial to evaluate the safety and immunogenicity of a two-dose primary vaccination series of monovalent A/Indonesia/5/2005 (H5N1) vaccine antigen adjuvanted with AS03 in children aged 6 months to < 18 years of age.

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2012-001683-29 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 26 January 2014 |

Results information

| | |
|--------------------------------|---|
| Result version number | v2 (current) |
| This version publication date | 30 July 2022 |
| First version publication date | 01 August 2015 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Correction of full data set and alignment between registries. |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 114464 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01310413 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | HHS O100200700029C: HHS/BARDA Contract Number |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | GlaxoSmithKline Biologicals |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330 |
| Public contact | Clinical Trails Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact | Clinical Trails Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.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? | Yes |

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 29 April 2014 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 21 July 2011 |
| Global end of trial reached? | Yes |
| Global end of trial date | 26 January 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess whether two doses of H5N1 antigen in association with AS03 adjuvant elicits an immune response, measured by postimmunization vaccine-homologous virus hemagglutination inhibition (HI) titers, that meets or exceeds Center for Biologics Evaluation and Research (CBER)/ Committee for Medicinal Products for Human Use (CHMP) young adult targets for proportion of subjects attaining postimmunization reciprocal HI titres ≥ 40 against A/Indonesia/5/2005 virus (abbreviated seroprotection rate [SPR].

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the time the subject consents to participate in the study until she/he is discharged.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 07 March 2011 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 2 Years |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 453 |
| Country: Number of subjects enrolled | Thailand: 292 |
| Country: Number of subjects enrolled | Canada: 97 |
| Worldwide total number of subjects | 842 |
| EEA total number of subjects | 0 |

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) | 274 |
| Children (2-11 years) | 568 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study included a first 385-days Blinded Phase (all subjects), followed by a 385-days Unblinded Phase. In this phase, subjects who received the placebo in the Blinded Phase were offered, after completing the Blinded Phase, 2 doses of Influenza A (H5N1) Virus monovalent vaccine administered for Dose 1 within a short delay of Day 385 (Day U0).

Pre-assignment

Screening details:

A total of 842 subjects were enrolled in the study in its Blinded Phase part. This number was later amended down to 838, following corrections for wrong subject number allocation and randomization errors.

Period 1

| | |
|------------------------------|---------------------------------|
| Period 1 title | Day 0 to Day 385 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Assessor |

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Influenza A (H5N1) adjuvanted 6-<36M Group |

Arm description:

Subjects aged at enrolment between 3 and 36 months, 36 months excluded, received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (>=) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Influenza A (H5N1) Virus monovalent vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Emulsion for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

All subjects will receive 2 doses administered as an intramuscular (IM) injection.

| | |
|------------------|---|
| Arm title | Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group |
|------------------|---|

Arm description:

Subjects aged at enrolment between 3 and 9 years, 9 years excluded, received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Influenza A (H5N1) Virus monovalent vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Emulsion for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

All subjects will receive 2 doses administered as an intramuscular (IM) injection.

| | |
|------------------|--|
| Arm title | Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group |
|------------------|--|

Arm description:

Subjects aged at enrolment between 9 and 18 years, 18 years excluded, received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Influenza A (H5N1) Virus monovalent vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Emulsion for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

All subjects will receive 2 doses administered as an intramuscular (IM) injection.

| | |
|------------------|----------------------|
| Arm title | Placebo 6-<36M Group |
|------------------|----------------------|

Arm description:

Subjects aged at enrolment between 3 and 36 months, 36 months excluded, received 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (>=) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

| | |
|--|------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Saline placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

All subjects will receive 2 doses administered as an intramuscular (IM) injection.

| | |
|------------------|---------------------|
| Arm title | Placebo 3-<9Y Group |
|------------------|---------------------|

Arm description:

Subjects aged at enrolment between 3 and 9 years, 9 years excluded, received 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

| | |
|--|------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Saline placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

All subjects will receive 2 doses administered as an intramuscular (IM) injection.

| | |
|------------------|----------------------|
| Arm title | Placebo 9-<18Y Group |
|------------------|----------------------|

Arm description:

Subjects aged at enrolment between 9 and 18 years, 18 years excluded, received 2 doses of saline

placebo at Days 0 and 21. The saline placebo was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

| | |
|--|------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Saline placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

All subjects will receive 2 doses administered as an intramuscular (IM) injection.

| Number of subjects in period 1 ^[1] | Influenza A (H5N1) adjuvanted 6-<36M Group | Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group |
|---|--|---|--|
| | | | |
| Started | 199 | 198 | 210 |
| Completed | 172 | 190 | 203 |
| Not completed | 27 | 8 | 7 |
| Consent withdrawn by subject | 5 | 2 | - |
| Migrated/moved from study are | 3 | 3 | 1 |
| Unspecified | 1 | - | 3 |
| Lost to follow-up | 18 | 3 | 3 |

| Number of subjects in period 1 ^[1] | Placebo 6-<36M Group | Placebo 3-<9Y Group | Placebo 9-<18Y Group |
|---|----------------------|---------------------|----------------------|
| | | | |
| Started | 75 | 76 | 80 |
| Completed | 67 | 73 | 77 |
| Not completed | 8 | 3 | 3 |
| Consent withdrawn by subject | 2 | 1 | 1 |
| Migrated/moved from study are | 1 | 1 | - |
| Unspecified | - | - | - |
| Lost to follow-up | 5 | 1 | 2 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 842 subjects were enrolled in the study in its Blinded Phase part. This number was later amended down to 838, following corrections for wrong subject number allocation and randomization errors.

Period 2

| | |
|------------------------------|--------------------|
| Period 2 title | Day Uo to Day U385 |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|--|---|
| Arm title | Placebo/Influenza A (H5N1) Adjuvanted Group |
| Arm description: | |
| Subjects in this group were those who were administered the saline placebo solution in the Blinded Phase of the study (either in the Placebo 6-<36M, Placebo 3-<9Y or Placebo 9-<18Y Group). These were subjects aged at enrolment between 6 months and 18 years, 18 years excluded, who had received 2 doses of saline placebo at Days 0 and 21 in the Blinded Phase of the study, as per described in the descriptions of the Placebo 6-<36M, Placebo 3-<9Y and Placebo 9-<18Y groups. After consenting to participating to the Unblinded Phase of the study, these subjects received in addition 2 doses of Influenza A (H5N1) Virus monovalent vaccine at Days 385 (Day U0) and Day 385 + 21 days (Day U21). Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly. Dose 1 was administered in the deltoid region of the non-dominant arm and Dose 2 in the deltoid region of the dominant arm. | |
| Arm type | Experimental |
| Investigational medicinal product name | Influenza A (H5N1) Virus monovalent vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Emulsion for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| All subjects will receive 2 doses administered as an intramuscular (IM) injection at Days U0 and U21. | |

| | |
|---|---|
| Number of subjects in period 2^[2] | Placebo/Influenza A (H5N1) Adjuvanted Group |
| Started | 155 |
| Completed | 152 |
| Not completed | 3 |
| Consent withdrawn by subject | 1 |
| Lost to follow-up | 2 |

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Out of the 782 subjects aged 6 months to <18 years that completed the Blinded phase of the study (Day 0 to Day 385), only 155 subjects consented to participate in the Unblinded phase of the study (Day U0 to Day U385). Thus, the number of subjects starting the period is not consistent with the number completing the preceding period.

Baseline characteristics

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Influenza A (H5N1) adjuvanted 6-<36M Group |
|-----------------------|--|

Reporting group description:

Subjects aged at enrolment between 3 and 36 months, 36 months excluded, received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (>=) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

| | |
|-----------------------|---|
| Reporting group title | Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group |
|-----------------------|---|

Reporting group description:

Subjects aged at enrolment between 3 and 9 years, 9 years excluded, received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

| | |
|-----------------------|--|
| Reporting group title | Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group |
|-----------------------|--|

Reporting group description:

Subjects aged at enrolment between 9 and 18 years, 18 years excluded, received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

| | |
|-----------------------|----------------------|
| Reporting group title | Placebo 6-<36M Group |
|-----------------------|----------------------|

Reporting group description:

Subjects aged at enrolment between 3 and 36 months, 36 months excluded, received 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (>=) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

| | |
|-----------------------|---------------------|
| Reporting group title | Placebo 3-<9Y Group |
|-----------------------|---------------------|

Reporting group description:

Subjects aged at enrolment between 3 and 9 years, 9 years excluded, received 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

| | |
|-----------------------|----------------------|
| Reporting group title | Placebo 9-<18Y Group |
|-----------------------|----------------------|

Reporting group description:

Subjects aged at enrolment between 9 and 18 years, 18 years excluded, received 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

| Reporting group values | Influenza A (H5N1) adjuvanted 6-<36M Group | Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group |
|------------------------|--|---|--|
| Number of subjects | 199 | 198 | 210 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | |

| | | | |
|--|----------------|-----------------|------------------|
| Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: months arithmetic mean standard deviation | 21.7 ± 8.17 | 70.5 ± 21.71 | 160.8 ± 28.21 |
| Gender categorical Units: Subjects | | | |
| Female | 92 | 90 | 103 |
| Male | 107 | 108 | 107 |

| Reporting group values | Placebo 6-<36M Group | Placebo 3-<9Y Group | Placebo 9-<18Y Group |
|--|----------------------|---------------------|----------------------|
| Number of subjects | 75 | 76 | 80 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: months arithmetic mean standard deviation | 22.6 ± 8.17 | 65.2 ± 20.2 | 156 ± 31.29 |
| Gender categorical Units: Subjects | | | |
| Female | 39 | 35 | 42 |
| Male | 36 | 41 | 38 |

| Reporting group values | Total | | |
|---|------------------|--|--|
| Number of subjects | 838 | | |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) | 0 0 0 0 | | |

| | | | |
|--|-----|--|--|
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age continuous Units: months arithmetic mean standard deviation | - | | |
| Gender categorical Units: Subjects | | | |
| Female | 401 | | |
| Male | 437 | | |

End points

End points reporting groups

| | |
|--|--|
| Reporting group title | Influenza A (H5N1) adjuvanted 6-<36M Group |
| Reporting group description: Subjects aged at enrolment between 3 and 36 months, 36 months excluded, received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (>=) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm). | |
| Reporting group title | Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group |
| Reporting group description: Subjects aged at enrolment between 3 and 9 years, 9 years excluded, received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm). | |
| Reporting group title | Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group |
| Reporting group description: Subjects aged at enrolment between 9 and 18 years, 18 years excluded, received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm). | |
| Reporting group title | Placebo 6-<36M Group |
| Reporting group description: Subjects aged at enrolment between 3 and 36 months, 36 months excluded, received 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (>=) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm). | |
| Reporting group title | Placebo 3-<9Y Group |
| Reporting group description: Subjects aged at enrolment between 3 and 9 years, 9 years excluded, received 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm). | |
| Reporting group title | Placebo 9-<18Y Group |
| Reporting group description: Subjects aged at enrolment between 9 and 18 years, 18 years excluded, received 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly, Dose 1 in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm). | |
| Reporting group title | Placebo/Influenza A (H5N1) Adjuvanted Group |
| Reporting group description: Subjects in this group were those who were administered the saline placebo solution in the Blinded Phase of the study (either in the Placebo 6-<36M, Placebo 3-<9Y or Placebo 9-<18Y Group). These were subjects aged at enrolment between 6 months and 18 years, 18 years excluded, who had received 2 doses of saline placebo at Days 0 and 21 in the Blinded Phase of the study, as per described in the descriptions of the Placebo 6-<36M, Placebo 3-<9Y and Placebo 9-<18Y groups. After consenting to participating to the Unblinded Phase of the study, these subjects received in addition 2 doses of Influenza A (H5N1) Virus monovalent vaccine at Days 385 (Day U0) and Day 385 + 21 days (Day U21). Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly. Dose 1 was administered in the deltoid region of the non-dominant arm and Dose 2 in the deltoid region of the dominant arm. | |

| | |
|----------------------------|-------------------------------------|
| Subject analysis set title | Influenza A (H5N1) adjuvanted Group |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

This group results from the pooling of the Influenza A (H5N1) adjuvanted 6-<36M, Influenza A (H5N1) adjuvanted 3-<9Y and Influenza A (H5N1) adjuvanted months and 18 years, 18 years excluded, who received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (\geq) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

| | |
|----------------------------|--------------------|
| Subject analysis set title | Placebo Group |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

This group results from the pooling of the Placebo 6-<36M, Placebo 3-<9Y and Placebo 9-<18Y groups and includes subjects aged at enrolment between 6 months and 18 years, 18 years excluded, who received 2 doses of 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (\geq) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

Primary: Number of subjects seroprotected for haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.

| | |
|-----------------|--|
| End point title | Number of subjects seroprotected for haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain. ^[1] |
|-----------------|--|

End point description:

A seroprotected subject against the a/Indonesia/5/2005 (A/INDO) virus strain was defined as a subject with H5N1 reciprocal haemagglutination inhibition (HI) antibody titers greater than or equal to (\geq) the seroprotection cut-off of 1:40.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

At Day 42.

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | Influenza A (H5N1) adjuvanted 6-<36M Group | Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group | Placebo 6-<36M Group |
|-----------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 175 | 185 | 203 | 64 |
| Units: Subjects | | | | |
| A/INDO, Day 42 | 175 | 184 | 201 | 0 |

| End point values | Placebo 3-<9Y Group | Placebo 9-<18Y Group | | |
|-----------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 76 | | |
| Units: Subjects | | | | |

| | | | | |
|----------------|---|---|--|--|
| A/INDO, Day 42 | 0 | 1 | | |
|----------------|---|---|--|--|

Statistical analyses

No statistical analyses for this end point

Primary: Haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain

| | |
|-----------------|--|
| End point title | Haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain ^[2] |
|-----------------|--|

End point description:

HI antibody titers against the H5N1 A/Indonesia virus strain (A/INDO) were expressed as geometric mean titers (GMTs). The cut-off of the assay was the seropositivity cut-off of higher than or equal to (\geq) 1:10.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

At Day 42.

Notes:

[2] - 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | Influenza A (H5N1) adjuvanted 6- <36M Group | Influenza A (H5N1) Virus monovalent vaccine 3- <9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9- <18Y Group | Placebo 6- <36M Group |
|--|---|--|---|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 175 | 185 | 203 | 64 |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| A/INDO, Day 42 | 777.1 (705.6 to 855.9) | 543.8 (484.9 to 609.8) | 416.2 (371.5 to 466.2) | 5.1 (4.9 to 5.3) |

| End point values | Placebo 3- <9Y Group | Placebo 9- <18Y Group | | |
|--|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 76 | | |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| A/INDO, Day 42 | 5.4 (5 to 5.7) | 5.8 (5.3 to 6.3) | | |

Statistical analyses

Secondary: Haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.

| | |
|-----------------|--|
| End point title | Haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain. |
|-----------------|--|

End point description:

HI antibody titers against the H5N1 A/Indonesia virus strain (A/INDO) were expressed as geometric mean titers (GMTs). The cut-off of the assay was the seropositivity cut-off of higher than or equal to (\geq) 1:10.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Days 0 and 21

| End point values | Influenza A (H5N1) adjuvanted 6- <36M Group | Influenza A (H5N1) Virus monovalent vaccine 3- <9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9- <18Y Group | Placebo 6- <36M Group |
|--|---|--|---|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 182 | 184 | 204 | 67 |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| A/INDO, Day 0 [N=182;184;204;67;71;76] | 5.3 (5.1 to 5.5) | 5.6 (5.3 to 5.9) | 5.7 (5.4 to 6.1) | 5.3 (5 to 5.7) |
| A/INDO, Day 21 [N=179;184;204;67;70;76] | 38.7 (33.9 to 44.2) | 44.6 (39.2 to 50.9) | 35.3 (31.7 to 39.5) | 5.2 (5 to 5.4) |

| End point values | Placebo 3- <9Y Group | Placebo 9- <18Y Group | | |
|--|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 76 | | |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| A/INDO, Day 0 [N=182;184;204;67;71;76] | 5.6 (5.1 to 6) | 5.4 (5.1 to 5.8) | | |
| A/INDO, Day 21 [N=179;184;204;67;70;76] | 5.4 (5 to 5.7) | 5.4 (5.1 to 5.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected for haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.

| | |
|-----------------|--|
| End point title | Number of subjects seroprotected for haemagglutination |
|-----------------|--|

inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.

End point description:

A seroprotected subject against the a/Indonesia/5/2005 (A/INDO) virus strain was defined as a subject with H5N1 reciprocal haemagglutination inhibition (HI) antibody titers greater than or equal to (\geq) the seroprotection cut-off of 1:40.

End point type Secondary

End point timeframe:

At Days 0 and 21

| End point values | Influenza A (H5N1) adjuvanted 6-<36M Group | Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group | Placebo 6-<36M Group |
|--|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 182 | 184 | 204 | 67 |
| Units: Subjects | | | | |
| A/INDO, Day 0 [N=182;184;204;67;71;76] | 1 | 2 | 1 | 0 |
| A/INDO, Day 21 [N=179;184;204;67;70;76] | 105 | 110 | 108 | 0 |

| End point values | Placebo 3-<9Y Group | Placebo 9-<18Y Group | | |
|--|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 76 | | |
| Units: Subjects | | | | |
| A/INDO, Day 0 [N=182;184;204;67;71;76] | 0 | 0 | | |
| A/INDO, Day 21 [N=179;184;204;67;70;76] | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Increase (GMI) for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain.

End point title Geometric Mean Increase (GMI) for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain.

End point description:

GMI also known as the seroconversion factor (SCF) or geometric mean fold rise (GMFR) was defined as the geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the pre-vaccination reciprocal HI titre for the vaccine virus.

End point type Secondary

End point timeframe:

At Days 21 and 42

| End point values | Influenza A (H5N1) adjuvanted 6-<36M Group | Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group | Placebo 6-<36M Group |
|--|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 179 | 185 | 204 | 67 |
| Units: Ratio | | | | |
| geometric mean (confidence interval 95%) | | | | |
| A/INDO, Day 21 [N=179;184;204;67;70;76] | 7.3 (6.4 to 8.4) | 8 (7 to 9.1) | 6.2 (5.5 to 6.9) | 1 (0.9 to 1) |
| A/INDO, Day 42 [N=175;185;203;64;71;76] | 148.5 (134.5 to 164.1) | 96.9 (85.3 to 110.1) | 72.4 (63.9 to 82) | 1 (0.9 to 1) |

| End point values | Placebo 3-<9Y Group | Placebo 9-<18Y Group | | |
|--|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 76 | | |
| Units: Ratio | | | | |
| geometric mean (confidence interval 95%) | | | | |
| A/INDO, Day 21 [N=179;184;204;67;70;76] | 1 (0.9 to 1) | 1 (0.9 to 1.1) | | |
| A/INDO, Day 42 [N=175;185;203;64;71;76] | 1 (0.9 to 1) | 1.1 (1 to 1.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.

| | |
|-----------------|--|
| End point title | Haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain. |
|-----------------|--|

End point description:

HI antibody titers against the H5N1 A/Indonesia virus strain (A/INDO) were expressed as geometric mean titers (GMTs). The cut-off of the assay was the seropositivity cut-off of higher than or equal to (\geq) 1:10. Adapted ATP cohort for immunogenicity included all evaluable subjects for which Day 21 and Day 42 data were obtained from the ATP cohort for immunogenicity at Day 42; Day 182 data were obtained from the ATP cohort for immunogenicity at Day 182, and Day 385 data were obtained from the ATP cohort for immunogenicity at Day 385.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Day 0 and Day 182.

| End point values | Influenza A (H5N1) adjuvanted 6- <36M Group | Influenza A (H5N1) Virus monovalent vaccine 3- <9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9- <18Y Group | Placebo 6- <36M Group |
|---|---|--|---|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 107 | 101 | 100 | 36 |
| Units: Titre | | | | |
| geometric mean (confidence interval 95%) | | | | |
| A/INDO, Day 0 [N=107;101;100;36;37;35] | 5.1 (5 to 5.2) | 5.2 (5 to 5.4) | 5.6 (5.2 to 6) | 5.3 (4.9 to 5.7) |
| A/INDO, Day 182 [N=84;89;87;29;34;31] | 90.6 (78.1 to 105) | 57.4 (50.8 to 64.9) | 50.2 (43.3 to 58.2) | 5 (5 to 5) |

| End point values | Placebo 3- <9Y Group | Placebo 9- <18Y Group | | |
|---|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 37 | 35 | | |
| Units: Titre | | | | |
| geometric mean (confidence interval 95%) | | | | |
| A/INDO, Day 0 [N=107;101;100;36;37;35] | 5.2 (4.8 to 5.8) | 5.4 (4.8 to 6) | | |
| A/INDO, Day 182 [N=84;89;87;29;34;31] | 5.4 (4.9 to 6) | 5.4 (4.9 to 5.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected as regards haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.

| | |
|-----------------|--|
| End point title | Number of subjects seroprotected as regards haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain. |
|-----------------|--|

End point description:

A seroprotected subject against the a/Indonesia/5/2005 (A/INDO) virus strain was defined as a subject with H5N1 reciprocal haemagglutination inhibition (HI) antibody titers greater than or equal to (\geq) the seroprotection cut-off of 1:40. As the analyses were performed and disclosed stepwise - i.e. as soon as a study phase was completed - several releases of the CTRS (result summaries) were published. To generate an integrated Clinical Study Report, one set of domain datasets covering all analyses was used and the Adapted ATP cohort for immunogenicity has been defined. As a consequence, some of the data previously disclosed and based on ATP cohort for immunogenicity at Day 42, Day 182 and Day 385 have been replaced in this summary with data generated with the Adapted ATP cohort for immunogenicity.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Day 0 and Day 182

| End point values | Influenza A (H5N1) adjuvanted 6- <36M Group | Influenza A (H5N1) Virus monovalent vaccine 3- <9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9- <18Y Group | Placebo 6- <36M Group |
|---|---|--|---|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 182 | 184 | 204 | 67 |
| Units: Subjects | | | | |
| A/INDO, Day 0 [N=182,184,204,67,71,76] | 1 | 2 | 1 | 0 |
| A/INDO, Day 182 [N=84;89;87;29;34;31] | 80 | 75 | 63 | 0 |

| End point values | Placebo 3- <9Y Group | Placebo 9- <18Y Group | | |
|---|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 76 | | |
| Units: Subjects | | | | |
| A/INDO, Day 0 [N=182,184,204,67,71,76] | 0 | 0 | | |
| A/INDO, Day 182 [N=84;89;87;29;34;31] | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain.

| | |
|-----------------|--|
| End point title | Number of seroconverted subjects for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain. |
|-----------------|--|

End point description:

A subject seroconverted for HI antibodies against the H5N1 A/Indonesia virus strain (A/INDO) was defined as a vaccinee with either a pre-vaccination titer less than (<) 1:10 and a post-vaccination titer higher than or equal to (>=) 1:40, or with a pre-vaccination titer >= 1:10 and at least a 4-fold increase in post-vaccination titer.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Day 182

| End point values | Influenza A (H5N1) adjuvanted 6-<36M Group | Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group | Placebo 6-<36M Group |
|-----------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 84 | 89 | 87 | 29 |
| Units: Subjects | | | | |
| A/INDO | 80 | 75 | 61 | 0 |

| End point values | Placebo 3-<9Y Group | Placebo 9-<18Y Group | | |
|-----------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 34 | 31 | | |
| Units: Subjects | | | | |
| A/INDO | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Increase (GMI) for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain.

| | |
|-----------------|---|
| End point title | Geometric Mean Increase (GMI) for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain. |
|-----------------|---|

End point description:

GMI also known as the seroconversion factor (SCF) or geometric mean fold rise (GMFR) was defined as the geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the pre-vaccination reciprocal HI titre for the vaccine virus.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Day 182

| End point values | Influenza A (H5N1) adjuvanted 6-<36M Group | Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group | Placebo 6-<36M Group |
|--|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 84 | 89 | 87 | 29 |
| Units: Ratio | | | | |
| geometric mean (confidence interval 95%) | | | | |
| A/INDO | 17.8 (15.3 to 20.8) | 11 (9.7 to 12.4) | 8.8 (7.5 to 10.4) | 1 (0.9 to 1) |

| End point values | Placebo 3-<9Y Group | Placebo 9-<18Y Group | | |
|--|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 34 | 31 | | |
| Units: Ratio | | | | |
| geometric mean (confidence interval 95%) | | | | |
| A/INDO | 1.1 (1 to 1.2) | 1 (0.9 to 1.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.

| | |
|-----------------|--|
| End point title | Haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain. |
|-----------------|--|

End point description:

HI antibody titers against the H5N1 A/Indonesia virus strain (A/INDO) were expressed as geometric mean titers (GMTs). The cut-off of the assay was the seropositivity cut-off of higher than or equal to (\geq) 1:10. As the analyses were performed and disclosed stepwise - i.e. as soon as a study phase was completed - several releases of the CTRS (result summaries) were published. To generate an integrated Clinical Study Report, one set of domain datasets covering all analyses was used and the Adapted ATP cohort for immunogenicity has been defined. As a consequence, some of the data previously disclosed and based on ATP cohort for immunogenicity at Day 42, Day 182 and Day 385 have been replaced in this summary with data generated with the Adapted ATP cohort for immunogenicity.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At Day 0 and Day 385 | |

| End point values | Influenza A (H5N1) adjuvanted 6-<36M Group | Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group | Placebo 6-<36M Group |
|---|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 182 | 184 | 204 | 67 |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| A/INDO, Day 0 [N=182;184;204;67;71;76] | 5.3 (5.1 to 5.5) | 5.6 (5.3 to 5.9) | 5.7 (5.4 to 6.1) | 5.3 (5 to 5.7) |
| A/INDO, Day 385 [N=63;85;95;26;34;36] | 65.6 (55.9 to 76.9) | 32.8 (28.1 to 38.4) | 21.6 (18.6 to 25.1) | 5.1 (4.9 to 5.4) |

| End point values | Placebo 3-<9Y Group | Placebo 9-<18Y Group | | |
|---|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 76 | | |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| A/INDO, Day 0 [N=182,184,204,67,71,76] | 5.6 (5.1 to 6) | 5.4 (5.1 to 5.8) | | |
| A/INDO, Day 385 [N=63;85;95;26;34;36] | 5.4 (4.9 to 5.8) | 5.3 (4.8 to 5.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected for haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain.

| | |
|--|---|
| End point title | Number of subjects seroprotected for haemagglutination inhibition (HI) antibody titers against the H5N1 A/Indonesia virus strain. |
| End point description: | |
| A seroprotected subject against the a/Indonesia/5/2005 (A/INDO) virus strain was defined as a subject with H5N1 reciprocal haemagglutination inhibition (HI) antibody titers greater than or equal to (\geq) the seroprotection cut-off of 1:40. As the analyses were performed and disclosed stepwise - i.e. as soon as a study phase was completed - several releases of the CTRS (result summaries) were published. To generate an integrated Clinical Study Report, one set of domain datasets covering all analyses was used and the Adapted ATP cohort for immunogenicity has been defined. As a consequence, some of the data previously disclosed and based on ATP cohort for immunogenicity at Day 42, Day 182 and Day 385 have been replaced in this summary with data generated with the Adapted ATP cohort for immunogenicity. | |
| End point type | Secondary |
| End point timeframe: | |
| At Day 0 and Day 385 | |

| End point values | Influenza A (H5N1) adjuvanted 6-<36M Group | Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group | Placebo 6-<36M Group |
|---|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 182 | 184 | 204 | 67 |
| Units: Subjects | | | | |
| A/INDO, Day 0 [N=182, 184,204,67,71,76] | 1 | 2 | 1 | 0 |
| A/INDO, Day 385 [N=63;85;95;26;34;36] | 54 | 47 | 27 | 0 |

| End point values | Placebo 3-<9Y Group | Placebo 9-<18Y Group | | |
|------------------|---------------------|----------------------|--|--|
|------------------|---------------------|----------------------|--|--|

| | | | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 76 | | |
| Units: Subjects | | | | |
| A/INDO, Day 0 [N=182, 184,204,67,71,76] | 0 | 0 | | |
| A/INDO, Day 385 [N=63;85;95;26;34;36] | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain.

| | |
|---|--|
| End point title | Number of seroconverted subjects for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain. |
| End point description: A subject seroconverted for HI antibodies against the H5N1 A/Indonesia virus strain (A/INDO) was defined as a vaccinee with either a pre-vaccination titer less than (<) 1:10 and a post-vaccination titer higher than or equal to (>=) 1:40, or with a pre-vaccination titer >= 1:10 and at least a 4-fold increase in post-vaccination titer. | |
| End point type | Secondary |
| End point timeframe: At Day 385 | |

| End point values | Influenza A (H5N1) adjuvanted 6-<36M Group | Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group | Placebo 6-<36M Group |
|-----------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 63 | 84 | 95 | 26 |
| Units: Subjects | | | | |
| A/INDO | 53 | 45 | 23 | 0 |

| End point values | Placebo 3-<9Y Group | Placebo 9-<18Y Group | | |
|-----------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 34 | 36 | | |
| Units: Subjects | | | | |
| A/INDO | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Increase (GMI) for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain.

| | |
|-----------------|---|
| End point title | Geometric Mean Increase (GMI) for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain. |
|-----------------|---|

End point description:

GMI also known as the seroconversion factor (SCF) or geometric mean fold rise (GMFR) was defined as the geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titer to the pre-vaccination reciprocal HI titer for the vaccine virus.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Day 385.

| End point values | Influenza A (H5N1) adjuvanted 6- <36M Group | Influenza A (H5N1) Virus monovalent vaccine 3- <9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9- <18Y Group | Placebo 6- <36M Group |
|--|---|--|---|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 63 | 85 | 95 | 26 |
| Units: Fold increase | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Fold increase | 12.1 (10.3 to 14.2) | 5.5 (4.7 to 6.6) | 3.6 (3.1 to 4.3) | 1 (0.9 to 1.1) |

| End point values | Placebo 3- <9Y Group | Placebo 9- <18Y Group | | |
|--|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 34 | 36 | | |
| Units: Fold increase | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Fold increase | 0.9 (0.8 to 1) | 1 (0.8 to 1.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Microneutralization (MN) antibody titers against the H5N1 A/Indonesia and H5N1 A/Vietnam virus strains.

| | |
|-----------------|---|
| End point title | Microneutralization (MN) antibody titers against the H5N1 A/Indonesia and H5N1 A/Vietnam virus strains. |
|-----------------|---|

End point description:

MN HI antibody titers against the H5N1 A/Indonesia (A/INDO) and H5N1 A/Vietnam (A/VIET) virus strains were expressed as geometric mean titers (GMTs). The cut-off of the assay was the seropositivity

cut-off of higher than or equal to (\geq) 1:28.

| | |
|----------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At Days 0, 42, 182 and 385 | |

| End point values | Influenza A (H5N1) adjuvanted 6- <36M Group | Influenza A (H5N1) Virus monovalent vaccine 3- <9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9- <18Y Group | Placebo 6- <36M Group |
|--|---|--|---|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 36 | 39 | 40 | 10 |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| A/INDO, Day 0 [N=36;37;40;7;10;11] | 14 (14 to 14) | 15.67 (14.37 to 17.08) | 15.54 (14.13 to 17.09) | 15.46 (12.13 to 19.7) |
| A/INDO, Day 42 [N=34;37;40;6;10;11] | 855.62 (597.88 to 1224.47) | 657.6 (453.13 to 954.33) | 380.62 (277.43 to 522.2) | 14 (14 to 14) |
| A/INDO, Day 182 [N=33;39;33;10;10;9] | 216.82 (162.03 to 290.14) | 130.32 (107.3 to 158.26) | 104.18 (86.95 to 124.82) | 16.11 (11.73 to 22.13) |
| A/INDO, Day 385 [N=25;33;37;8;11;9] | 166.64 (135.9 to 204.32) | 108.59 (87.88 to 134.19) | 82.26 (67.27 to 100.59) | 15.27 (12.44 to 18.74) |
| A/VIET, Day 0 [N=36;36;40;7;10;11] | 14.83 (13.89 to 15.84) | 19.84 (16.82 to 23.4) | 24.88 (20.75 to 29.85) | 17.11 (10.47 to 27.95) |
| A/VIET, Day 42 [N=34;37;40;6;10;11] | 68.18 (58.05 to 80.07) | 71.15 (61.62 to 82.15) | 65.25 (57.03 to 74.64) | 17.69 (9.69 to 32.28) |
| A/VIET, Day 182 [N=33;39;33;10;10;9] | 48.77 (36.56 to 65.06) | 44.11 (36.19 to 53.77) | 61.67 (51.38 to 74.01) | 19.82 (12.22 to 32.14) |
| A/VIET, Day 385 [N=25;33;37;8;11;9] | 59.83 (48.09 to 74.43) | 38.62 (30.6 to 48.73) | 47.73 (38.76 to 58.79) | 14 (14 to 14) |

| End point values | Placebo 3- <9Y Group | Placebo 9- <18Y Group | | |
|--|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 11 | 11 | | |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| A/INDO, Day 0 [N=36;37;40;7;10;11] | 14 (14 to 14) | 14.91 (12.96 to 17.16) | | |
| A/INDO, Day 42 [N=34;37;40;6;10;11] | 14 (14 to 14) | 14.91 (12.96 to 17.16) | | |
| A/INDO, Day 182 [N=33;39;33;10;10;9] | 14 (14 to 14) | 17.67 (12.08 to 25.86) | | |
| A/INDO, Day 385 [N=25;33;37;8;11;9] | 14.91 (12.96 to 17.16) | 16.33 (12.91 to 20.66) | | |
| A/VIET, Day 0 [N=36;36;40;7;10;11] | 16.08 (13.05 to 19.82) | 20.47 (14.82 to 28.26) | | |
| A/VIET, Day 42 [N=34;37;40;6;10;11] | 19.87 (12.97 to 30.43) | 28.14 (19.53 to 40.54) | | |

| | | | | |
|--------------------------------------|------------------------|------------------------|--|--|
| A/VIET, Day 182 [N=33;39;33;10;10;9] | 17.24 (13.56 to 21.9) | 24.14 (14.29 to 40.78) | | |
| A/VIET, Day 385 [N=25;33;37;8;11;9] | 18.07 (12.34 to 26.47) | 35.42 (19.45 to 64.49) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Vaccine response rate (VRR) for microneutralization (MN) antibodies against the H5N1 A/Indonesia and H5N1 A/Vietnam virus strains.

| | |
|-----------------|--|
| End point title | Vaccine response rate (VRR) for microneutralization (MN) antibodies against the H5N1 A/Indonesia and H5N1 A/Vietnam virus strains. |
|-----------------|--|

End point description:

A subject with a vaccine response was defined either as a seronegative subject with an antibody titre < 1:28 for H5N1 Flu A/Indonesia MN and H5N1 A/Vietnam or as a seropositive subject with an antibody titre ≥ 1:28 for H5N1 Flu A/Indonesia MN and H5N1 A/Vietnam. VRR for MN was defined as the incidence rate of vaccinees with a 4-fold increase in post vaccination reciprocal titer relative to Day 0.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Day 42

| End point values | Influenza A (H5N1) adjuvanted 6-<36M Group | Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group | Placebo 6-<36M Group |
|-----------------------------|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 34 | 37 | 40 | 6 |
| Units: Subjects | | | | |
| A/INDO [N=34;37;40;6;10;11] | 34 | 37 | 39 | 0 |
| A/VIET [N=34;36;40;6;10;11] | 30 | 26 | 16 | 0 |

| End point values | Placebo 3-<9Y Group | Placebo 9-<18Y Group | | |
|-----------------------------|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 11 | 11 | | |
| Units: Subjects | | | | |
| A/INDO [N=34;37;40;6;10;11] | 0 | 0 | | |
| A/VIET [N=34;36;40;6;10;11] | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local symptoms.

| | |
|-----------------|--|
| End point title | Number of subjects reporting solicited local symptoms. |
|-----------------|--|

End point description:

Solicited local symptoms assessed were pain, redness and swelling. "Any" was defined as any occurrence of the specified solicited local symptom reported, regardless of intensity. Grade 3 pain was defined as pain that prevented normal activity. Grade 3 redness and swelling were defined as redness/swelling above 100 millimeter (mm).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the 7-day (Days 0-6) post-vaccination periods post Doses 1 and 2 of vaccine/placebo, across doses (Year 1)

| End point values | Influenza A (H5N1) adjuvanted Group | Placebo Group | | |
|-----------------------------|-------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 603 | 229 | | |
| Units: Subjects | | | | |
| Any pain | 405 | 69 | | |
| Grade 3 pain | 25 | 4 | | |
| Any redness | 29 | 0 | | |
| Grade 3 redness | 1 | 0 | | |
| Any swelling | 41 | 1 | | |
| Grade 3 swelling | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local symptoms.

| | |
|-----------------|--|
| End point title | Number of subjects reporting solicited local symptoms. |
|-----------------|--|

End point description:

Solicited local symptoms assessed were pain and swelling. "Any" was defined as any occurrence of the specified solicited local symptom reported, regardless of intensity. Grade 3 pain was defined as pain that prevented normal activity. Grade 3 redness and swelling were defined as redness/swelling above 100 millimeter (mm).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the 7-day (Days U0-U6) post-vaccination periods post Doses 1 and 2 of vaccine/placebo, across doses (Year 2)

| End point values | Placebo/Influenza A (H5N1) Adjuvanted Group | | | |
|-----------------------------|---|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 154 | | | |
| Units: Subjects | | | | |
| Any Pain | 111 | | | |
| Grade 3 Pain | 8 | | | |
| Any Redness | 6 | | | |
| Grade 3 Redness | 0 | | | |
| Any Swelling | 5 | | | |
| Grade 3 Swelling | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects of less than 6 years of age reporting solicited general symptoms

| | |
|-----------------|---|
| End point title | Number of subjects of less than 6 years of age reporting solicited general symptoms |
|-----------------|---|

End point description:

Solicited general symptoms assessed in subjects of less than 6 years of age were drowsiness, irritability/fussiness, loss of appetite and fever [axillary temperature (T) higher than or equal to (\geq) 38.0 degrees Celsius ($^{\circ}$ C)]. "Any" was defined as any occurrence of the specified solicited general symptom reported, regardless of intensity or relationship to vaccination. Grade 3 was defined as a general symptom that prevented normal activity. Related was defined as a general symptom assessed by the investigator as causally related to the study vaccination. Any fever was defined as axillary temperature above 38.0 degrees Celsius ($^{\circ}$ C). Grade 3 fever was axillary temperature above 39.0 $^{\circ}$ C.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the 7-day (Days 0-6) post-vaccination periods post Doses 1 and 2 of vaccine/placebo, across doses (Year 1)

| End point values | Influenza A (H5N1) adjuvanted Group | Placebo Group | | |
|--------------------------------|-------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 294 | 122 | | |
| Units: Subjects | | | | |
| Any Drowsiness | 101 | 29 | | |
| Grade 3 Drowsiness | 9 | 2 | | |
| Related Drowsiness | 81 | 21 | | |
| Any Irritability/fussiness | 128 | 40 | | |
| Grade 3 Irritability/fussiness | 10 | 2 | | |
| Related Irritability/fussiness | 111 | 33 | | |
| Any Loss of appetite | 79 | 29 | | |
| Grade 3 Loss of appetite | 8 | 4 | | |
| Related Loss of appetite | 63 | 20 | | |

| | | | | |
|--------------------------------------|----|----|--|--|
| Any Fever (Axillary T \geq 38.0°C) | 59 | 21 | | |
| Grade 3 Fever | 14 | 5 | | |
| Related Fever | 41 | 14 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects of less than 6 years of age reporting solicited general symptoms

| | |
|-----------------|---|
| End point title | Number of subjects of less than 6 years of age reporting solicited general symptoms |
|-----------------|---|

End point description:

Solicited general symptoms assessed in subjects of less than 6 years of age were drowsiness, irritability/fussiness, loss of appetite and fever [axillary temperature (T) higher than or equal to (\geq) 38.0 degrees Celsius (°C)]. "Any" was defined as any occurrence of the specified solicited general symptom reported, regardless of intensity or relationship to vaccination. Grade 3 was defined as a general symptom that prevented normal activity. Related was defined as a general symptom assessed by the investigator as causally related to the study vaccination. Any fever was defined as axillary temperature above 38.0 degrees Celsius (°C). Grade 3 fever was axillary temperature above 39.0°C.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the 7-day (Days U0-U6) post-vaccination periods post Doses 1 and 2 of vaccine/placebo, for each dose (Year 2)

| End point values | Placebo/Influenza A (H5N1) Adjuvanted Group | | | |
|--------------------------------|---|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 79 | | | |
| Units: Subjects | | | | |
| Any Drowsiness | 23 | | | |
| Grade 3 Drowsiness | 1 | | | |
| Related Drowsiness | 17 | | | |
| Any Irritability/Fussiness | 28 | | | |
| Grade 3 Irritability/Fussiness | 1 | | | |
| Related Irritability/Fussiness | 23 | | | |
| Any Loss of appetite | 18 | | | |
| Grade 3 Loss of appetite | 0 | | | |
| Related Loss of appetite | 13 | | | |
| Any Fever | 4 | | | |
| Grade 3 Fever | 2 | | | |
| Related Fever | 3 | | | |

Statistical analyses

Secondary: Number of subjects at least 6 years of age reporting solicited general symptoms

| | |
|-----------------|---|
| End point title | Number of subjects at least 6 years of age reporting solicited general symptoms |
|-----------------|---|

End point description:

Solicited general symptoms assessed in subjects of at least 6 years of age were fatigue, gastrointestinal symptoms, headache, joint pain at other location, muscle aches, shivering, sweating and fever [axillary temperature (T) ≥ 38.0 degrees Celsius ($^{\circ}\text{C}$)]. Gastrointestinal symptoms included nausea, vomiting, diarrhea and/or abdominal pain. "Any" was defined as any occurrence of the specified solicited general symptom reported, regardless of intensity or relationship to vaccination. Grade 3 was defined as a general symptom that prevented normal activity. Related was defined as a general symptom assessed by the investigator as causally related to the study vaccination.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the 7-day (Days 0-6) post-vaccination periods post Doses 1 and 2 of vaccine/placebo, across doses (Year 1)

| End point values | Influenza A (H5N1) adjuvanted Group | Placebo Group | | |
|--|-------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 309 | 107 | | |
| Units: Subjects | | | | |
| Any fatigue | 89 | 19 | | |
| Grade 3 fatigue | 4 | 2 | | |
| Related fatigue | 77 | 16 | | |
| Any gastrointestinal symptoms | 43 | 18 | | |
| Grade 3 gastrointestinal symptoms | 4 | 2 | | |
| Related gastrointestinal symptoms | 27 | 11 | | |
| Any headache | 100 | 18 | | |
| Grade 3 headache | 8 | 3 | | |
| Related headache | 87 | 15 | | |
| Any joint pain | 50 | 9 | | |
| Grade 3 joint pain | 2 | 0 | | |
| Related joint pain | 43 | 8 | | |
| Any muscle aches | 123 | 17 | | |
| Grade 3 muscle aches | 7 | 1 | | |
| Related muscle aches | 114 | 14 | | |
| Any shivering | 25 | 7 | | |
| Grade 3 shivering | 2 | 1 | | |
| Related shivering | 19 | 5 | | |
| Any sweating | 25 | 4 | | |
| Grade 3 sweating | 2 | 0 | | |
| Related sweating | 22 | 1 | | |
| Any fever [axillary temperature ≥ 38.0 $^{\circ}\text{C}$] | 19 | 3 | | |
| Grade 3 fever | 5 | 1 | | |
| Related fever | 13 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects at least 6 years of age reporting solicited general symptoms

| | |
|-----------------|---|
| End point title | Number of subjects at least 6 years of age reporting solicited general symptoms |
|-----------------|---|

End point description:

Solicited general symptoms assessed in subjects of at least 6 years of age were fatigue, gastrointestinal symptoms, headache, joint pain at other location, muscle aches, shivering, sweating and fever [axillary temperature (T) ≥ 38.0 degrees Celsius ($^{\circ}\text{C}$)]. Gastrointestinal symptoms included nausea, vomiting, diarrhea and/or abdominal pain. "Any" was defined as any occurrence of the specified solicited general symptom reported, regardless of intensity or relationship to vaccination. Grade 3 was defined as a general symptom that prevented normal activity. Related was defined as a general symptom assessed by the investigator as causally related to the study vaccination.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the 7-day (Days U0-U6) post-vaccination periods post Doses 1 and 2 of vaccine/placebo, for each dose (Year 2)

| End point values | Placebo/Influenza A (H5N1) Adjuvanted Group | | | |
|-----------------------------|---|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 75 | | | |
| Units: Subjects | | | | |
| Any Fatigue | 18 | | | |
| Grade 3 Fatigue | 1 | | | |
| Related Fatigue | 13 | | | |
| Any Gastrointestinal | 7 | | | |
| Grade 3 Gastrointestinal | 0 | | | |
| Related Gastrointestinal | 5 | | | |
| Any Headache | 24 | | | |
| Grade 3 Headache | 1 | | | |
| Related Headache | 20 | | | |
| Any Increased Sweating | 5 | | | |
| Grade 3 Increased Sweating | 0 | | | |
| Related Increased Sweating | 3 | | | |
| Any Joint Pain | 14 | | | |
| Grade 3 Joint Pain | 0 | | | |
| Related Joint Pain | 12 | | | |
| Any Muscle Aches | 34 | | | |
| Grade 3 Muscle Aches | 0 | | | |
| Related Muscle Aches | 28 | | | |

| | | | | |
|----------------------------|---|--|--|--|
| Any Shivering (Chills) | 7 | | | |
| Grade 3 Shivering (Chills) | 2 | | | |
| Related Shivering (Chills) | 4 | | | |
| Any Fever | 1 | | | |
| Grade 3 Fever | 0 | | | |
| Related Fever | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with medically-attended adverse events (MAEs)

| | |
|-----------------|--|
| End point title | Number of subjects with medically-attended adverse events (MAEs) |
|-----------------|--|

End point description:

MAEs were defined as adverse events with medically-attended visits that were not routine visits for physical examination or vaccination. Any MAE was defined as at least 1 MAE experienced.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 0 up to Day 385

| End point values | Influenza A (H5N1) adjuvanted Group | Placebo Group | | |
|-----------------------------|-------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 607 | 231 | | |
| Units: Subjects | | | | |
| Subject(s) with any MAE(s) | 189 | 77 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with medically-attended adverse events (MAEs)

| | |
|-----------------|--|
| End point title | Number of subjects with medically-attended adverse events (MAEs) |
|-----------------|--|

End point description:

MAEs were defined as adverse events with medically-attended visits that were not routine visits for physical examination or vaccination. Any MAE was defined as at least 1 MAE experienced.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day U0 up to Day U385

| End point values | Placebo/Influenza A (H5N1) Adjuvanted Group | | | |
|-----------------------------|---|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155 | | | |
| Units: Subjects | | | | |
| Any MAEs | 36 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any potential Immune-Mediated Diseases (pIMDs)

| | |
|-----------------|--|
| End point title | Number of subjects with any potential Immune-Mediated Diseases (pIMDs) |
|-----------------|--|

End point description:

Potential immune-mediated diseases (pIMDs) were defined as a subset of adverse events that included both clearly autoimmune diseases and also other inflammatory and/or neurologic disorders which might or might not have an autoimmune aetiology. "Any pIMD" was defined as at least one pIMD experienced by the study subject.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 0 up to Day 385

| End point values | Influenza A (H5N1) adjuvanted Group | Placebo Group | | |
|-----------------------------|-------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 607 | 231 | | |
| Units: Subjects | | | | |
| Subject(s) with any pIMD(s) | 1 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any potential Immune-Mediated Diseases (pIMDs)

| | |
|-----------------|--|
| End point title | Number of subjects with any potential Immune-Mediated Diseases (pIMDs) |
|-----------------|--|

End point description:

Potential immune-mediated diseases (pIMDs) were defined as a subset of adverse events that included both clearly autoimmune diseases and also other inflammatory and/or neurologic disorders which might or might not have an autoimmune aetiology. "Any pIMD" was defined as at least one pIMD experienced by the study subject.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day U0 to Day U385

| End point values | Placebo/Influenza A (H5N1) Adjuvanted Group | | | |
|-----------------------------|---|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155 | | | |
| Units: Subjects | | | | |
| Subjects with any pIMD(s) | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting pregnancies, and outcomes of these reported pregnancies

| | |
|-----------------|--|
| End point title | Number of subjects reporting pregnancies, and outcomes of these reported pregnancies |
|-----------------|--|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 0 up to Day 385

| End point values | Influenza A (H5N1) adjuvanted Group | Placebo Group | | |
|-----------------------------------|-------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 607 | 231 | | |
| Units: Subjects | | | | |
| Subject(s) with any pregnancy | 2 | 0 | | |
| Subject(s) with related pregnancy | 0 | 0 | | |
| Spontaneous abortion | 1 | 0 | | |
| Healthy live birth | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting pregnancies, and outcomes of these reported pregnancies

| | |
|-----------------|--|
| End point title | Number of subjects reporting pregnancies, and outcomes of these reported pregnancies |
|-----------------|--|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day U0 up to Day U385

| End point values | Placebo/Influenza A (H5N1) Adjuvanted Group | | | |
|-------------------------------|---|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155 | | | |
| Units: Subjects | | | | |
| Subject(s) with any pregnancy | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with normal and abnormal biochemical parameters assessed with respect to alanine aminotransferase (ALAT) and aspartate aminotransferase (ASAT)

| | |
|-----------------|---|
| End point title | Number of subjects with normal and abnormal biochemical parameters assessed with respect to alanine aminotransferase (ALAT) and aspartate aminotransferase (ASAT) |
|-----------------|---|

End point description:

Subjects were categorized according to their results at pre-vaccination (PRE), Day 42, Day 182 and Day 385 which were normal, above normal, below the normal ranges or unknown.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 0 up to Day 385

| End point values | Influenza A (H5N1) adjuvanted Group | Placebo Group | | |
|-----------------------------|-------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 606 | 231 | | |
| Units: Subjects | | | | |

| | | | | |
|-----------------------------------|-----|-----|--|--|
| ALAT, PRE Unknown [N=606,231] | 15 | 4 | | |
| ALAT, PRE Below [N=606,231] | 0 | 0 | | |
| ALAT, PRE Normal [N=606,231] | 586 | 221 | | |
| ALAT, PRE Above [N=606,231] | 5 | 6 | | |
| ALAT, Day 42 Unknown [N=583,220] | 17 | 4 | | |
| ALAT, Day 42 Below [N=583,220] | 0 | 0 | | |
| ALAT, Day 42 Normal [N=583,220] | 562 | 212 | | |
| ALAT, Day 42 Above [N=583,220] | 4 | 4 | | |
| ALAT, Day 182 Unknown [N=304,110] | 6 | 0 | | |
| ALAT, Day 182 Below [N=304,110] | 0 | 0 | | |
| ALAT, Day 182 Normal [N=304,110] | 289 | 110 | | |
| ALAT, Day 182 Above [N=304,110] | 9 | 0 | | |
| ALAT, Day 385 Unknown [N=251,104] | 5 | 0 | | |
| ALAT, Day 385 Below [N=251,104] | 0 | 0 | | |
| ALAT, Day 385 Normal [N=251,104] | 245 | 100 | | |
| ALAT, Day 385 Above [N=251,104] | 1 | 4 | | |
| ASAT, PRE Unknown [N=606,231] | 15 | 4 | | |
| ASAT, PRE Below [N=606,231] | 0 | 0 | | |
| ASAT, PRE Normal [N=606,231] | 577 | 219 | | |
| ASAT, PRE Above [N=606,231] | 14 | 8 | | |
| ASAT, Day 42 Unknown [N=583,220] | 19 | 4 | | |
| ASAT, Day 42 Below [N=583,220] | 0 | 0 | | |
| ASAT, Day 42 Normal [N=583,220] | 552 | 208 | | |
| ASAT, Day 42 Above [N=583,220] | 12 | 8 | | |
| ASAT, Day 182 Unknown [N=304,110] | 8 | 0 | | |
| ASAT, Day 182 Below [N=304,110] | 0 | 0 | | |
| ASAT, Day 182 Normal [N=304,110] | 284 | 108 | | |
| ASAT, Day 182 Above [N=304,110] | 12 | 2 | | |
| ASAT, Day 385 Unknown [N=251,104] | 7 | 0 | | |
| ASAT, Day 385 Below [N=251,104] | 0 | 0 | | |
| ASAT, Day 385 Normal [N=251,104] | 240 | 100 | | |
| ASAT, Day 385 Above [N=251,104] | 4 | 4 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with normal and abnormal biochemical parameters assessed with respect to total bilirubin (T-BIL) and bilirubin conjugated/direct (BIL-C/D)

| | |
|-----------------|---|
| End point title | Number of subjects with normal and abnormal biochemical parameters assessed with respect to total bilirubin (T-BIL) and bilirubin conjugated/direct (BIL-C/D) |
|-----------------|---|

End point description:

Subjects were categorized according to their results at pre-vaccination (PRE), Day 42, Day 182 and Day 385 which were normal, above normal, below the normal ranges or unknown.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 0 up to Day 385

| End point values | Influenza A (H5N1) adjuvanted Group | Placebo Group | | |
|---|--|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 606 | 231 | | |
| Units: Subjects | | | | |
| T-BIL, PRE Unknown [N=606,231] | 15 | 4 | | |
| T-BIL, PRE Below [N=606,231] | 0 | 0 | | |
| T-BIL, PRE Normal [N=606,231] | 587 | 224 | | |
| T-BIL, PRE Above [N=606,231] | 4 | 3 | | |
| T-BIL, Day 42 Unknown [N=583,220] | 16 | 4 | | |
| T-BIL, Day 42 Below [N=583,220] | 0 | 0 | | |
| T-BIL, Day 42 Normal [N=583,220] | 558 | 214 | | |
| T-BIL, Day 42 Above [N=583,220] | 9 | 2 | | |
| T-BIL, Day 182 Unknown [N=304,110] | 6 | 0 | | |
| T-BIL, Day 182 Below [N=304,110] | 0 | 0 | | |
| T-BIL, Day 182 Normal [N=304,110] | 296 | 110 | | |
| T-BIL, Day 182 Above [N=304,110] | 2 | 0 | | |
| T-BIL, Day 385 Unknown [N=251,104] | 7 | 1 | | |
| T-BIL, Day 385 Below [N=251,104] | 0 | 0 | | |
| T-BIL, Day 385 Normal [N=251,104] | 240 | 102 | | |
| T-BIL, Day 385 Above [N=251,104] | 4 | 1 | | |
| BIL-C/D, PRE Unknown [N=606,231] | 15 | 4 | | |
| BIL-C/D, PRE Below [N=606,231] | 0 | 0 | | |
| BIL-C/D, PRE Normal [N=606,231] | 591 | 226 | | |
| BIL-C/D, PRE Above [N=606,231] | 0 | 1 | | |
| BIL-C/D, Day 42 Unknown [N=583,220] | 16 | 4 | | |
| BIL-C/D, Day 42 Below [N=583,220] | 0 | 0 | | |
| BIL-C/D, Day 42 Normal [N=583,220] | 558 | 214 | | |
| BIL-C/D, Day 42 Above [N=583,220] | 9 | 2 | | |
| BIL-C/D, Day 182 Unknown [N=304,110] | 7 | 0 | | |
| BIL-C/D, Day 182 Below [N=304,110] | 0 | 0 | | |
| BIL-C/D, Day 182 Normal [N=304,110] | 297 | 110 | | |
| BIL-C/D, Day 182 Above [N=304,110] | 0 | 0 | | |
| BIL-C/D, Day 385 Unknown [N=251,104] | 8 | 1 | | |
| BIL-C/D, Day 385 Below [N=251,104] | 0 | 0 | | |
| BIL-C/D, Day 385 Normal [N=251,104] | 240 | 103 | | |
| BIL-C/D, Day 385 Above [N=251,104] | 3 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs).

| | |
|--|--|
| End point title | Number of subjects reporting any unsolicited adverse events (AEs). |
| End point description: An unsolicited AE was defined as any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. "Any" was defined as occurrence of any unsolicited symptom regardless of intensity grade or relation to vaccination. | |
| End point type | Secondary |
| End point timeframe: During the 21-day (Days 0-20) post-vaccination period following Dose 1 of vaccine/placebo | |

| End point values | Influenza A (H5N1) adjuvanted Group | Placebo Group | | |
|-------------------------------------|-------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 607 | 231 | | |
| Units: Subjects | | | | |
| Subject(s) with any unsolicited AEs | 153 | 63 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs).

| | |
|--|--|
| End point title | Number of subjects reporting any unsolicited adverse events (AEs). |
| End point description: An unsolicited AE was defined as any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. "Any" was defined as occurrence of any unsolicited symptom regardless of intensity grade or relation to vaccination. | |
| End point type | Secondary |
| End point timeframe: During the 21-day (Days 21-41) post-vaccination period following Dose 2 of vaccine/placebo | |

| End point values | Influenza A (H5N1) adjuvanted Group | Placebo Group | | |
|-------------------------------------|-------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 593 | 224 | | |
| Units: Subjects | | | | |
| Subject(s) with any unsolicited AEs | 135 | 54 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs).

| | |
|-----------------|--|
| End point title | Number of subjects reporting any unsolicited adverse events (AEs). |
|-----------------|--|

End point description:

An unsolicited AE was defined as any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. "Any" was defined as occurrence of any unsolicited symptom regardless of intensity grade or relation to vaccination.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the 42-day (Days 0-41) post-vaccination period following Dose 1 of vaccine/placebo

| End point values | Influenza A (H5N1) adjuvanted Group | Placebo Group | | |
|-------------------------------------|-------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 607 | 231 | | |
| Units: Subjects | | | | |
| Subject(s) with any unsolicited AEs | 243 | 97 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events (SAEs)

| | |
|-----------------|--|
| End point title | Number of subjects reporting serious adverse events (SAEs) |
|-----------------|--|

End point description:

A SAE was defined as any untoward medical occurrence that: resulted in death, was life threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity or was a congenital anomaly/birth defect in the offspring of a study subject. Any was defined as occurrence of any symptom regardless of intensity grade or relation to vaccination and related was an event assessed by the investigator as causally related to the study vaccination.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 0 up to Day 385

| End point values | Influenza A (H5N1) adjuvanted Group | Placebo Group | | |
|-----------------------------|-------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 607 | 231 | | |
| Units: Subjects | | | | |
| Subject(s) with any SAE(s) | 8 | 4 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events (SAEs)

| | |
|--|--|
| End point title | Number of subjects reporting serious adverse events (SAEs) |
| End point description: A SAE was defined as any untoward medical occurrence that: resulted in death, was life threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity or was a congenital anomaly/birth defect in the offspring of a study subject. Any was defined as occurrence of any symptom regardless of intensity grade or relation to vaccination and related was an event assessed by the investigator as causally related to the study vaccination. | |
| End point type | Secondary |
| End point timeframe: From Day U0 up to Day U385 | |

| End point values | Placebo/Influenza A (H5N1) Adjuvanted Group | | | |
|-----------------------------|---|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155 | | | |
| Units: Subjects | | | | |
| Subject(s) with any SAE(s) | 2 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs).

| | |
|--|--|
| End point title | Number of subjects reporting any unsolicited adverse events (AEs). |
| End point description: An unsolicited AE was defined as any AE (i.e. any untoward medical occurrence in a patient or clinical | |

investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. "Any" was defined as occurrence of any unsolicited symptom regardless of intensity grade or relation to vaccination.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the 21-day (Days U0-U20) post-vaccination period following Dose 1 of Influenza A (H5N1) Virus monovalent vaccine

| | | | | |
|-------------------------------------|---|--|--|--|
| End point values | Placebo/Influenza A (H5N1) Adjuvanted Group | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155 | | | |
| Units: Subjects | | | | |
| Subject(s) with any unsolicited AEs | 21 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs).

| | |
|-----------------|--|
| End point title | Number of subjects reporting any unsolicited adverse events (AEs). |
|-----------------|--|

End point description:

An unsolicited AE was defined as any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. "Any" was defined as occurrence of any unsolicited symptom regardless of intensity grade or relation to vaccination.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the 21-day (Days U21-U41) post-vaccination period following Dose 2 of Influenza A (H5N1) Virus monovalent vaccine

| | | | | |
|-------------------------------------|---|--|--|--|
| End point values | Placebo/Influenza A (H5N1) Adjuvanted Group | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155 | | | |
| Units: Subjects | | | | |
| Subject(s) with any unsolicited AEs | 27 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs).

| | |
|-----------------|--|
| End point title | Number of subjects reporting any unsolicited adverse events (AEs). |
|-----------------|--|

End point description:

An unsolicited AE was defined as any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. "Any" was defined as occurrence of any unsolicited symptom regardless of intensity grade or relation to vaccination.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the 42-day (Days U0-U41) post-vaccination period following Dose 1 of Influenza A (H5N1) Virus monovalent vaccine

| | | | | |
|-------------------------------------|---|--|--|--|
| End point values | Placebo/Influenza A (H5N1) Adjuvanted Group | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 155 | | | |
| Units: Subjects | | | | |
| Subject(s) with any unsolicited AEs | 41 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with normal and abnormal biochemical parameters assessed with respect to creatinine (CREA) and blood urea nitrogen (BUN)

| | |
|-----------------|---|
| End point title | Number of subjects with normal and abnormal biochemical parameters assessed with respect to creatinine (CREA) and blood urea nitrogen (BUN) |
|-----------------|---|

End point description:

Subjects were categorized according to their results at pre-vaccination (PRE), Day 42, Day 182 and Day 385 which were normal, above normal, below the normal ranges or unknown.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 0 up to Day 385

| End point values | Influenza A (H5N1) adjuvanted Group | Placebo Group | | |
|-----------------------------------|-------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 607 | 231 | | |
| Units: Subjects | | | | |
| CREA, PRE Unknown [N=606,231] | 15 | 4 | | |
| CREA, PRE Below [N=606, 231] | 142 | 61 | | |
| CREA, PRE Within [N=606, 231] | 447 | 165 | | |
| CREA, PRE Above [N=606, 231] | 2 | 1 | | |
| CREA, Day 42 Unknown [N=583,220] | 17 | 4 | | |
| CREA, Day 42 Below [N=583,220] | 130 | 48 | | |
| CREA, Day 42 Within [N=583,220] | 432 | 166 | | |
| CREA, Day 42 Above [N=583,220] | 4 | 2 | | |
| CREA, Day 182 Unknown [N=304,110] | 6 | 1 | | |
| CREA, Day 182 Below [N=304,110] | 66 | 26 | | |
| CREA, Day 182 Within [N=304,110] | 231 | 83 | | |
| CREA, Day 182 Above [N=304,110] | 1 | 0 | | |
| CREA, Day 385 Unknown [N=251,104] | 6 | 0 | | |
| CREA, Day 385 Below [N=251,104] | 51 | 24 | | |
| CREA, Day 385 Within [N=251,104] | 191 | 80 | | |
| CREA, Day 385 Above [N=251,104] | 3 | 0 | | |
| BUN, PRE Unknown [N=606,231] | 15 | 4 | | |
| BUN, PRE Below [N=606,231] | 13 | 4 | | |
| BUN, PRE Within [N=606,231] | 553 | 218 | | |
| BUN, PRE Above [N=606,231] | 25 | 5 | | |
| BUN, Day 42 Unknown [N=583,220] | 17 | 4 | | |
| BUN, Day 42 Below [N=583,220] | 11 | 3 | | |
| BUN, Day 42 Within [N=583,220] | 531 | 209 | | |
| BUN, Day 42 Above [N=583,220] | 24 | 4 | | |
| BUN, Day 182 Unknown [N=304,110] | 6 | 0 | | |
| BUN, Day 182 Below [N=304,110] | 8 | 2 | | |
| BUN, Day 182 Within [N=304,110] | 281 | 105 | | |
| BUN, Day 182 Above [N=304,110] | 9 | 3 | | |
| BUN, Day 385 Unknown [N=251,104] | 7 | 0 | | |
| BUN, Day 385 Below [N=251,104] | 3 | 2 | | |
| BUN, Day 385 Within [N=251,104] | 237 | 100 | | |
| BUN, Day 385 Above [N=251,104] | 4 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with normal and abnormal haematological parameters assessed with respect to basophils (BAS) and eosinophils (EOS)

| | |
|---|--|
| End point title | Number of subjects with normal and abnormal haematological parameters assessed with respect to basophils (BAS) and eosinophils (EOS) |
| End point description: | |
| Subjects were categorized according to their results at pre-vaccination (PRE), Day 42, Day 182 and Day 385 which were normal, above normal, below the normal ranges or unknown. | |
| End point type | Secondary |
| End point timeframe: | |
| From Day 0 up to Day 385 | |

| End point values | Influenza A (H5N1) adjuvanted Group | Placebo Group | | |
|----------------------------------|-------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 607 | 231 | | |
| Units: Subjects | | | | |
| BAS, PRE Unknown [N=606,231] | 29 | 12 | | |
| BAS, PRE Below [N=606,231] | 0 | 0 | | |
| BAS, PRE Within [N=606,231] | 576 | 219 | | |
| BAS, PRE Above [N=606,231] | 1 | 0 | | |
| BAS, Day 42 Unknown [N=583,220] | 34 | 13 | | |
| BAS, Day 42 Below [N=583,220] | 0 | 0 | | |
| BAS, Day 42 Within [N=583,220] | 549 | 207 | | |
| BAS, Day 42 Above [N=583,220] | 0 | 0 | | |
| BAS, Day 182 Unknown [N=304,110] | 17 | 2 | | |
| BAS, Day 182 Below [N=304,110] | 0 | 0 | | |
| BAS, Day 182 Within [N=304,110] | 287 | 108 | | |
| BAS, Day 182 Above [N=304,110] | 0 | 0 | | |
| BAS, Day 385 Unknown [N=251,104] | 6 | 3 | | |
| BAS, Day 385 Below [N=251,104] | 0 | 0 | | |
| BAS, Day 385 Within [N=251,104] | 245 | 101 | | |
| BAS, Day 385 Above [N=251,104] | 0 | 0 | | |
| EOS, PRE Unknown [N=606,231] | 29 | 12 | | |
| EOS, PRE Below [N=606,231] | 68 | 19 | | |
| EOS, PRE Within [N=606,231] | 473 | 187 | | |
| EOS, PRE Above [N=606,231] | 36 | 13 | | |
| EOS, Day 42 Unknown [N=583,220] | 34 | 13 | | |
| EOS, Day 42 Below [N=583,220] | 49 | 15 | | |
| EOS, Day 42 Within [N=583,220] | 452 | 175 | | |
| EOS, Day 42 Above [N=583,220] | 48 | 17 | | |
| EOS, Day 182 Unknown [N=304,110] | 17 | 2 | | |
| EOS, Day 182 Below [N=304,110] | 33 | 11 | | |
| EOS, Day 182 Within [N=304,110] | 237 | 85 | | |
| EOS, Day 182 Above [N=304,110] | 17 | 12 | | |
| EOS, Day 385 Unknown [N=251,104] | 6 | 3 | | |
| EOS, Day 385 Below [N=251,104] | 32 | 17 | | |
| EOS, Day 385 Within [N=251,104] | 198 | 77 | | |
| EOS, Day 385 Above [N=251,104] | 15 | 7 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with normal and abnormal haematological parameters assessed with respect to haematocrit (Hcr) and haemoglobin (Hgb)

| | |
|-----------------|--|
| End point title | Number of subjects with normal and abnormal haematological parameters assessed with respect to haematocrit (Hcr) and haemoglobin (Hgb) |
|-----------------|--|

End point description:

Subjects were categorized according to their results at pre-vaccination (PRE), Day 42, Day 182 and Day 385 which were normal, above normal, below the normal ranges or unknown.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 0 up to Day 385

| End point values | Influenza A (H5N1) adjuvanted Group | Placebo Group | | |
|----------------------------------|-------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 607 | 231 | | |
| Units: Subjects | | | | |
| Hcr, PRE Unknown [N=606,231] | 26 | 10 | | |
| Hcr, PRE Below [N=606,231] | 53 | 21 | | |
| Hcr, PRE Within [N=606,231] | 480 | 181 | | |
| Hcr, PRE Above [N=606,231] | 47 | 19 | | |
| Hcr, Day 42 Unknown [N=583,220] | 19 | 7 | | |
| Hcr, Day 42 Below [N=583,220] | 45 | 13 | | |
| Hcr, Day 42 Within [N=583,220] | 477 | 178 | | |
| Hcr, Day 42 Above [N=583,220] | 42 | 22 | | |
| Hcr, Day 182 Unknown [N=304,110] | 12 | 2 | | |
| Hcr, Day 182 Below [N=304,110] | 38 | 7 | | |
| Hcr, Day 182 Within [N=304,110] | 238 | 91 | | |
| Hcr, Day 182 Above [N=304,110] | 16 | 10 | | |
| Hcr, Day 385 Unknown [N=251,104] | 5 | 3 | | |
| Hcr, Day 385 Below [N=251,104] | 18 | 12 | | |
| Hcr, Day 385 Within [N=251,104] | 215 | 85 | | |
| Hcr, Day 385 Above [N=251,104] | 13 | 4 | | |
| Hgb, PRE Unknown [N=606,231] | 26 | 10 | | |
| Hgb, PRE Below [N=606,231] | 61 | 26 | | |
| Hgb, PRE Within [N=606,231] | 497 | 182 | | |
| Hgb, PRE Above [N=606,231] | 22 | 13 | | |
| Hgb, Day 42 Unknown [N=583,220] | 19 | 8 | | |

| | | | | |
|----------------------------------|-----|-----|--|--|
| Hgb, Day 42 Below [N=583,220] | 69 | 19 | | |
| Hgb, Day 42 Within [N=583,220] | 476 | 185 | | |
| Hgb, Day 42 Above [N=583,220] | 19 | 8 | | |
| Hgb, Day 182 Unknown [N=304,110] | 11 | 2 | | |
| Hgb, Day 182 Below [N=304,110] | 42 | 16 | | |
| Hgb, Day 182 Within [N=304,110] | 241 | 89 | | |
| Hgb, Day 182 Above [N=304,110] | 10 | 3 | | |
| Hgb, Day 385 Unknown [N=251,104] | 5 | 3 | | |
| Hgb, Day 385 Below [N=251,104] | 27 | 15 | | |
| Hgb, Day 385 Within [N=251,104] | 210 | 84 | | |
| Hgb, Day 385 Above [N=251,104] | 9 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with normal and abnormal haematological parameters assessed with respect to neutrophils (NEU) and platelets (PLA)

| | |
|-----------------|--|
| End point title | Number of subjects with normal and abnormal haematological parameters assessed with respect to neutrophils (NEU) and platelets (PLA) |
|-----------------|--|

End point description:

Subjects were categorized according to their results at pre-vaccination (PRE), Day 42, Day 182 and Day 385 which were normal, above normal, below the normal ranges or unknown.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 0 up to Day 385

| End point values | Influenza A (H5N1) adjuvanted Group | Placebo Group | | |
|----------------------------------|-------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 607 | 231 | | |
| Units: Subjects | | | | |
| NEU, PRE Unknown [N=606,231] | 29 | 12 | | |
| NEU, PRE Below [N=606,231] | 26 | 10 | | |
| NEU, PRE Within [N=606,231] | 534 | 202 | | |
| NEU, PRE Above [N=606,231] | 17 | 7 | | |
| NEU, Day 42 Unknown [N=583,220] | 34 | 13 | | |
| NEU, Day 42 Below [N=583,220] | 29 | 8 | | |
| NEU, Day 42 Within [N=583,220] | 505 | 189 | | |
| NEU, Day 42 Above [N=583,220] | 15 | 10 | | |
| NEU, Day 182 Unknown [N=304,110] | 17 | 2 | | |
| NEU, Day 182 Below [N=304,110] | 14 | 3 | | |
| NEU, Day 182 Within [N=304,110] | 266 | 105 | | |
| NEU, Day 182 Above [N=304,110] | 7 | 0 | | |
| NEU, Day 385 Unknown [N=251,104] | 6 | 3 | | |

| | | | | |
|----------------------------------|-----|-----|--|--|
| NEU, Day 385 Below [N=251,104] | 12 | 3 | | |
| NEU, Day 385 Within [N=251,104] | 227 | 96 | | |
| NEU, Day 385 Above [N=251,104] | 6 | 2 | | |
| PLA, PRE Unknown [N=606,231] | 35 | 17 | | |
| PLA, PRE Below [N=606,231] | 3 | 0 | | |
| PLA, PRE Within [N=606,231] | 518 | 187 | | |
| PLA, PRE Above [N=606,231] | 50 | 27 | | |
| PLA, Day 42 Unknown [N=583,220] | 32 | 12 | | |
| PLA, Day 42 Below [N=583,220] | 1 | 0 | | |
| PLA, Day 42 Within [N=583,220] | 500 | 184 | | |
| PLA, Day 42 Above [N=583,220] | 50 | 24 | | |
| PLA, Day 182 Unknown [N=304,110] | 20 | 5 | | |
| PLA, Day 182 Below [N=304,110] | 0 | 0 | | |
| PLA, Day 182 Within [N=304,110] | 260 | 96 | | |
| PLA, Day 182 Above [N=304,110] | 24 | 9 | | |
| PLA, Day 385 Unknown [N=251,104] | 8 | 8 | | |
| PLA, Day 385 Below [N=251,104] | 1 | 0 | | |
| PLA, Day 385 Within [N=251,104] | 234 | 94 | | |
| PLA, Day 385 Above [N=251,104] | 8 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with normal and abnormal haematological parameters assessed with respect to lymphocytes (LYM) and monocytes (MON)

| | |
|------------------------|---|
| End point title | Number of subjects with normal and abnormal haematological parameters assessed with respect to lymphocytes (LYM) and monocytes (MON) |
| End point description: | Subjects were categorized according to their results at pre-vaccination (PRE), Day 42, Day 182 and Day 385 which were normal, above normal, below the normal ranges or unknown. |
| End point type | Secondary |
| End point timeframe: | From Day 0 up to Day 385 |

| End point values | Influenza A (H5N1) adjuvanted Group | Placebo Group | | |
|---------------------------------|-------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 607 | 231 | | |
| Units: Subjects | | | | |
| LYM, PRE Unknown [N=606,231] | 29 | 12 | | |
| LYM, PRE Below [N=606,231] | 7 | 1 | | |
| LYM, PRE Within [N=606,231] | 441 | 161 | | |
| LYM, PRE Above [N=606,231] | 129 | 57 | | |
| LYM, Day 42 Unknown [N=583,220] | 34 | 13 | | |

| | | | | |
|----------------------------------|-----|-----|--|--|
| LYM, Day 42 Below [N=583,220] | 6 | 2 | | |
| LYM, Day 42 Within [N=583,220] | 446 | 162 | | |
| LYM, Day 42 Above [N=583,220] | 97 | 43 | | |
| LYM, Day 182 Unknown [N=304,110] | 17 | 2 | | |
| LYM, Day 182 Below [N=304,110] | 0 | 1 | | |
| LYM, Day 182 Within [N=304,110] | 235 | 93 | | |
| LYM, Day 182 Above [N=304,110] | 52 | 14 | | |
| LYM, Day 385 Unknown [N=251,104] | 6 | 3 | | |
| LYM, Day 385 Below [N=251,104] | 0 | 0 | | |
| LYM, Day 385 Within [N=251,104] | 223 | 86 | | |
| LYM, Day 385 Above [N=251,104] | 22 | 15 | | |
| MON, PRE Unknown [N=606,231] | 29 | 12 | | |
| MON, PRE Below [N=606,231] | 94 | 46 | | |
| MON, PRE Within [N=606,231] | 480 | 170 | | |
| MON, PRE Above [N=606,231] | 3 | 3 | | |
| MON, Day 42 Unknown [N=583,220] | 34 | 13 | | |
| MON, Day 42 Below [N=583,220] | 110 | 37 | | |
| MON, Day 42 Within [N=583,220] | 434 | 167 | | |
| MON, Day 42 Above [N=583,220] | 5 | 3 | | |
| MON, Day 182 Unknown [N=304,110] | 17 | 2 | | |
| MON, Day 182 Below [N=304,110] | 61 | 20 | | |
| MON, Day 182 Within [N=304,110] | 221 | 88 | | |
| MON, Day 182 Above [N=304,110] | 5 | 0 | | |
| MON, Day 385 Unknown [N=251,104] | 6 | 3 | | |
| MON, Day 385 Below [N=251,104] | 31 | 18 | | |
| MON, Day 385 Within [N=251,104] | 211 | 83 | | |
| MON, Day 385 Above [N=251,104] | 3 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with normal and abnormal haematological parameters assessed with respect to red and white blood cells (RBC and WBC)

| | |
|-----------------|--|
| End point title | Number of subjects with normal and abnormal haematological parameters assessed with respect to red and white blood cells (RBC and WBC) |
|-----------------|--|

End point description:

Subjects were categorized according to their results at pre-vaccination (PRE), Day 42, Day 182 and Day 385 which were normal, above normal, below the normal ranges or unknown.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 0 up to Day 385

| End point values | Influenza A (H5N1) adjuvanted Group | Placebo Group | | |
|----------------------------------|-------------------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 607 | 231 | | |
| Units: Subjects | | | | |
| RBC, PRE Unknown [N=606,231] | 26 | 10 | | |
| RBC, PRE Below [N=606,231] | 25 | 4 | | |
| RBC, PRE Within [N=606,231] | 504 | 198 | | |
| RBC, PRE Above [N=606,231] | 51 | 19 | | |
| RBC, Day 42 Unknown [N=583,220] | 19 | 8 | | |
| RBC, Day 42 Below [N=583,220] | 21 | 6 | | |
| RBC, Day 42 Within [N=583,220] | 496 | 189 | | |
| RBC, Day 42 Above [N=583,220] | 47 | 17 | | |
| RBC, Day 182 Unknown [N=304,110] | 11 | 2 | | |
| RBC, Day 182 Below [N=304,110] | 13 | 5 | | |
| RBC, Day 182 Within [N=304,110] | 266 | 93 | | |
| RBC, Day 182 Above [N=304,110] | 14 | 10 | | |
| RBC, Day 385 Unknown [N=251,104] | 5 | 3 | | |
| RBC, Day 385 Below [N=251,104] | 8 | 2 | | |
| RBC, Day 385 Within [N=251,104] | 214 | 90 | | |
| RBC, Day 385 Above [N=251,104] | 24 | 9 | | |
| WBC, PRE Unknown [N=606,231] | 29 | 12 | | |
| WBC, PRE Below [N=606,231] | 27 | 9 | | |
| WBC, PRE Within [N=606,231] | 543 | 207 | | |
| WBC, PRE Above [N=606,231] | 7 | 3 | | |
| WBC, Day 42 Unknown [N=583,220] | 34 | 13 | | |
| WBC, Day 42 Below [N=583,220] | 38 | 8 | | |
| WBC, Day 42 Within [N=583,220] | 508 | 198 | | |
| WBC, Day 42 Above [N=583,220] | 3 | 1 | | |
| WBC, Day 182 Unknown [N=304,110] | 17 | 2 | | |
| WBC, Day 182 Below [N=304,110] | 21 | 7 | | |
| WBC, Day 182 Within [N=304,110] | 264 | 101 | | |
| WBC, Day 182 Above [N=304,110] | 2 | 0 | | |
| WBC, Day 385 Unknown [N=251,104] | 6 | 3 | | |
| WBC, Day 385 Below [N=251,104] | 15 | 6 | | |
| WBC, Day 385 Within [N=251,104] | 230 | 94 | | |
| WBC, Day 385 Above [N=251,104] | 0 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive for microneutralization (MN) antibodies against the H5N1 A/Indonesia virus strain.

| | |
|-----------------|--|
| End point title | Number of subjects seropositive for microneutralization (MN) antibodies against the H5N1 A/Indonesia virus strain. |
|-----------------|--|

End point description:

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At Days 0 and 42 | |

| End point values | Influenza A (H5N1) adjuvanted 6- <36M Group | Influenza A (H5N1) Virus monovalent vaccine 3- <9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9- <18Y Group | Placebo 6- <36M Group |
|-----------------------------|---|--|---|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 36 | 37 | 40 | 7 |
| Units: Subjects | | | | |
| At Day 0 | 0 | 6 | 5 | 1 |
| At Day 42 | 34 | 37 | 40 | 0 |

| End point values | Placebo 3- <9Y Group | Placebo 9- <18Y Group | | |
|-----------------------------|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 10 | 11 | | |
| Units: Subjects | | | | |
| At Day 0 | 0 | 1 | | |
| At Day 42 | 0 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain

| | |
|-----------------|---|
| End point title | Number of seroconverted subjects for haemagglutination inhibition (HI) antibodies against the H5N1 A/Indonesia virus strain |
|-----------------|---|

End point description:

A subject seroconverted for HI antibodies against the H5N1 A/Indonesia virus strain (A/INDO) was defined as a vaccinee with either a pre-vaccination titer less than (<) 1:10 and a post-vaccination titer higher than or equal to (>=) 1:40, or with a pre-vaccination titer >= 1:10 and at least a 4-fold increase in post-vaccination titer. As the analyses were performed and disclosed stepwise - i.e. as soon as a study phase was completed - several releases of the CTRS (result summaries) were published. To generate an integrated Clinical Study Report, one set of domain datasets covering all analyses was used and the Adapted ATP cohort for immunogenicity has been defined. As a consequence, some of the data previously disclosed and based on ATP cohort for immunogenicity at Day 42, Day 182 and Day 385 have been replaced in this summary with data generated with the Adapted ATP cohort for immunogenicity.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At Days 21 and 42 | |

| End point values | Influenza A (H5N1) adjuvanted 6-<36M Group | Influenza A (H5N1) Virus monovalent vaccine 3-<9Y Group | Influenza A (H5N1) Virus monovalent vaccine 9-<18Y Group | Placebo 6-<36M Group |
|--|--|---|--|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 179 | 185 | 204 | 67 |
| Units: Subjects | | | | |
| A/INDO, Day 21 [N=179;183;204;67;70;76] | 103 | 107 | 105 | 0 |
| A/INDO, Day 42 [N=175;184;203;64;71;76] | 175 | 183 | 201 | 0 |

| End point values | Placebo 3-<9Y Group | Placebo 9-<18Y Group | | |
|--|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 76 | | |
| Units: Subjects | | | | |
| A/INDO, Day 21 [N=179;183;204;67;70;76] | 0 | 0 | | |
| A/INDO, Day 42 [N=175;184;203;64;71;76] | 0 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse events (SAE) = Day 0 to Day 385 and Day U0 to U385. Solicited local and general symptoms = During the 7-day period post vaccine/placebo administration. Unsolicited AEs = During the 42-day post vaccine/placebo administration.

Adverse event reporting additional description:

For the systematically assessed other (non-serious) adverse events, number of participants at risk included those from Total Vaccinated cohort who had the symptom sheet completed. The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 15.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------------------------|
| Reporting group title | Influenza A (H5N1) adjuvanted Group |
|-----------------------|-------------------------------------|

Reporting group description:

This group results from the pooling of the Influenza A (H5N1) adjuvanted 6-<36M, Influenza A (H5N1) adjuvanted 3-<9Y and Influenza A (H5N1) adjuvanted 9-<18Y groups and includes subjects aged at enrolment between 6 months and 18 years, 18 years excluded, who received 2 doses of Influenza A (H5N1) Virus monovalent vaccine (GSK1557484A vaccine or GSK Biologicals' monovalent A/Indonesia/5/2005 (H5N1) vaccine adjuvanted) at Days 0 and 21. Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (>=) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

| | |
|-----------------------|---|
| Reporting group title | Placebo/Influenza A (H5N1) adjuvanted Group |
|-----------------------|---|

Reporting group description:

Subjects in this group were those who were administered the saline placebo solution in the Blinded Phase of the study (either in the Placebo 6-<36M, Placebo 3-<9Y or Placebo 9-<18Y Group). These were subjects aged at enrolment between 6 months and 18 years, 18 years excluded, who had received 2 doses of saline placebo at Days 0 and 21 in the Blinded Phase of the study, as per described in the descriptions of the Placebo 6-<36M, Placebo 3-<9Y and Placebo 9-<18Y groups. After consenting to participating to the Unblinded Phase of the study, these subjects received in addition 2 doses of Influenza A (H5N1) Virus monovalent vaccine at Days 385 (Day U0) and Day 385 + 21 days (Day U21). Influenza A (H5N1) Virus monovalent vaccine was administered intramuscularly. Dose 1 of was administered in the deltoid region of the non-dominant arm and Dose 2 in the deltoid region of the dominant arm.

| | |
|-----------------------|---------------|
| Reporting group title | Placebo Group |
|-----------------------|---------------|

Reporting group description:

This group results from the pooling of the Placebo 6-<36M, Placebo 3-<9Y and Placebo 9-<18Y groups and includes subjects aged at enrolment between 6 months and 18 years, 18 years excluded, who received 2 doses of 2 doses of saline placebo at Days 0 and 21. The saline placebo was administered intramuscularly. For children aged up to 12 months, 12 months excluded (< 12 months), Dose 1 was administered in the left anterolateral thigh and Dose 2 in the right anterolateral thigh. For children older than (>=) 12 months, Dose 1 was administered in the deltoid region of the non-dominant arm (or left arm if dominance was not yet identified) and Dose 2 in the deltoid region of the dominant arm (or right arm).

| Serious adverse events | Influenza A (H5N1) adjuvanted Group | Placebo/Influenza A (H5N1) adjuvanted Group | Placebo Group |
|---|-------------------------------------|---|-----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 8 / 607 (1.32%) | 2 / 155 (1.29%) | 4 / 231 (1.73%) |

| | | | |
|---|--|-----------------|-----------------|
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Skeletal injury | Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group. | | |
| subjects affected / exposed | 1 / 607 (0.16%) | 0 / 155 (0.00%) | 0 / 231 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound | Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group. | | |
| subjects affected / exposed | 0 / 607 (0.00%) | 1 / 155 (0.65%) | 0 / 231 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Febrile convulsion | Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group. | | |
| subjects affected / exposed | 1 / 607 (0.16%) | 0 / 155 (0.00%) | 0 / 231 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group. | | |
| subjects affected / exposed | 1 / 607 (0.16%) | 0 / 155 (0.00%) | 0 / 231 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Lymphadenitis | Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group. | | |
| subjects affected / exposed | 0 / 607 (0.00%) | 0 / 155 (0.00%) | 1 / 231 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Inguinal hernia | Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group. | | |
| subjects affected / exposed | 1 / 607 (0.16%) | 0 / 155 (0.00%) | 0 / 231 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|--|-----------------|-----------------|
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group. | | |
| subjects affected / exposed | 0 / 607 (0.00%) | 0 / 155 (0.00%) | 1 / 231 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchial hyperreactivity | Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group. | | |
| subjects affected / exposed | 1 / 607 (0.16%) | 0 / 155 (0.00%) | 0 / 231 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Suicidal ideation | Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group. | | |
| subjects affected / exposed | 0 / 607 (0.00%) | 0 / 155 (0.00%) | 1 / 231 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Infectious mononucleosis | Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group. | | |
| subjects affected / exposed | 2 / 607 (0.33%) | 0 / 155 (0.00%) | 0 / 231 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group. | | |
| subjects affected / exposed | 1 / 607 (0.16%) | 0 / 155 (0.00%) | 0 / 231 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group. | | |
| subjects affected / exposed | 1 / 607 (0.16%) | 0 / 155 (0.00%) | 0 / 231 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group. | | |

| | | | |
|---|--|-----------------|-----------------|
| subjects affected / exposed | 1 / 607 (0.16%) | 0 / 155 (0.00%) | 0 / 231 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Scarlet fever | Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group. | | |
| subjects affected / exposed | 0 / 607 (0.00%) | 1 / 155 (0.65%) | 0 / 231 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group. | | |
| subjects affected / exposed | 1 / 607 (0.16%) | 0 / 155 (0.00%) | 0 / 231 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Type 1 diabetes mellitus | Additional description: SAE assessed during Day 0 to Day 385 for Influenza A (H5N1) adjuvanted and Placebo Groups and from Day U0 to U385 for the Placebo/Influenza A (H5N1) adjuvanted Group. | | |
| subjects affected / exposed | 0 / 607 (0.00%) | 0 / 155 (0.00%) | 1 / 231 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | Influenza A (H5N1) adjuvanted Group | Placebo/Influenza A (H5N1) adjuvanted Group | Placebo Group |
|---|-------------------------------------|---|--------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 502 / 607 (82.70%) | 124 / 155 (80.00%) | 189 / 231 (81.82%) |
| General disorders and administration site conditions | | | |
| Pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[1] | 405 / 603 (67.16%) | 111 / 154 (72.08%) | 69 / 229 (30.13%) |
| occurrences (all) | 405 | 111 | 69 |
| Swelling | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[2] | 41 / 603 (6.80%) | 5 / 154 (3.25%) | 1 / 229 (0.44%) |
| occurrences (all) | 41 | 5 | 1 |
| Drowsiness | | | |

| | | | |
|--|--------------------|------------------|-------------------|
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[3] | 101 / 294 (34.35%) | 23 / 79 (29.11%) | 29 / 122 (23.77%) |
| occurrences (all) | 101 | 23 | 29 |
| Irritability/fussiness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[4] | 128 / 294 (43.54%) | 28 / 79 (35.44%) | 40 / 122 (32.79%) |
| occurrences (all) | 128 | 28 | 40 |
| Loss of appetite | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[5] | 79 / 294 (26.87%) | 18 / 79 (22.78%) | 29 / 122 (23.77%) |
| occurrences (all) | 79 | 18 | 29 |
| Fever (axillary temperature \geq 38.0°C) (children less than 6 years of age) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[6] | 59 / 294 (20.07%) | 4 / 79 (5.06%) | 21 / 122 (17.21%) |
| occurrences (all) | 59 | 4 | 21 |
| Fatigue | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[7] | 89 / 309 (28.80%) | 18 / 75 (24.00%) | 19 / 107 (17.76%) |
| occurrences (all) | 89 | 18 | 19 |
| Gastrointestinal disorders | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[8] | 43 / 309 (13.92%) | 7 / 75 (9.33%) | 18 / 107 (16.82%) |
| occurrences (all) | 42 | 7 | 17 |
| Headache | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[9] | 100 / 309 (32.36%) | 24 / 75 (32.00%) | 18 / 107 (16.82%) |
| occurrences (all) | 100 | 24 | 18 |
| Joint pain at other location | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[10] | 50 / 309 (16.18%) | 14 / 75 (18.67%) | 9 / 107 (8.41%) |
| occurrences (all) | 50 | 14 | 9 |
| Muscle aches | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|--|--------------------|------------------|-------------------|
| subjects affected / exposed ^[11] | 123 / 309 (39.81%) | 34 / 75 (45.33%) | 17 / 107 (15.89%) |
| occurrences (all) | 123 | 34 | 17 |
| Shivering | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[12] | 25 / 309 (8.09%) | 7 / 75 (9.33%) | 7 / 107 (6.54%) |
| occurrences (all) | 25 | 7 | 7 |
| Sweating | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[13] | 25 / 309 (8.09%) | 5 / 75 (6.67%) | 4 / 107 (3.74%) |
| occurrences (all) | 25 | 5 | 4 |
| Fever (axillary temperature \geq 38.0°C) (children with at least 6 years of age) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[14] | 19 / 309 (6.15%) | 1 / 75 (1.33%) | 3 / 107 (2.80%) |
| occurrences (all) | 19 | 1 | 3 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 13 / 607 (2.14%) | 3 / 155 (1.94%) | 12 / 231 (5.19%) |
| occurrences (all) | 15 | 3 | 14 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 36 / 607 (5.93%) | 9 / 155 (5.81%) | 17 / 231 (7.36%) |
| occurrences (all) | 36 | 9 | 17 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 27 / 607 (4.45%) | 3 / 155 (1.94%) | 13 / 231 (5.63%) |
| occurrences (all) | 27 | 3 | 13 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 29 / 607 (4.78%) | 10 / 155 (6.45%) | 18 / 231 (7.79%) |
| occurrences (all) | 29 | 10 | 18 |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

medications, respectively).

[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 15 September 2010 | At the request of the U.S. Center for Biologics Research (CBER): (1) an independent data monitoring committee (IDMC) replaces the internal Safety Review Committee (iSRC) described in the previous version of the protocol, and (2) a blood sample for immunogenicity assessment has been added at the Day 21 visit. To facilitate receipt of immune-response information by participating study sites before epochs 4 and 5 begin, unblinding will occur after completion of the Day 182 visit. The language describing randomization of supplies has been modified to clarify that the vaccine will be presented in multi-dose vials that will be used as monodose vials in this study. Finally, several minor editorial errors have been corrected. |
| 08 December 2010 | The total volume of blood collected on Days 0, 42, and 182 or 385 has been decreased from 8.5 mL to 7 mL. The total volume of blood collected on Day 21 has been increased from 3.5 mL to 5 mL. These changes reflect a decrease in blood volume for safety laboratory assessments from 5 mL to 2 mL, as only a 2 mL sample is required by the central laboratory performing the tests. The total volume of blood collected for immune response assessments has been increased to 5 mL rather than 3.5 mL to allow for expanded testing for cross-reactive antibodies. Unblinding at the subject level will take place following the Day 385 analysis, as earlier unblinding potentially compromises assessment of adverse events during the interval between Days 183 and 385. A limit has been placed on the amount of time that may elapse following Day 385 during which placebo subjects may receive open-label, AS03-adjuvanted Q-PAN H5N1 vaccine. A table replaces the list of potential immune mediated diseases in Section 8.3.2.5. Minor editorial changes have also been made. |
| 11 April 2011 | Subject (family) unblinding will occur for each subject after completion of RDE, following the Day 385 contact, so the investigator can communicate treatment assignments to facilitate start of the unblinded portion of study (2nd year) for subjects who received placebo. Day U0 no longer can start on the same day as Day 385 due to the process by which unblinding at the subject level occurs. The process for allocation of subjects to a time point for the fourth blood sampling has been clarified. Assignment to a visit (and fourth blood sampling) at Day 182 and a phone call at Day 385 or the opposite will occur through an algorithm outside the randomization system and will be relayed to the investigator through the RDE system. The requirement for assessment of blood pressure during the Day 0/Screening visit physical exam has been removed, to align with clinical practice. In study procedure (Table 2), the activity "Randomization" had been inadvertently omitted and now has been added. In study procedure (Table 2), footnote # 10 was added to note that families with more than one child in the study may choose to have the follow-up phone contact for one child by interview at the time of the sibling's follow-up clinic visit (provided timings are within specified windows). To align study procedures (Table 3) with Section 5.7.3, the activity "Physical Exam" has been removed and the activity "Targeted physical exam, prn" has been added to Visit U1 (Day U0). In study procedures (Table 3), the activity "Targeted physical exam, prn" has been removed from Day U7 and Day U28 because these are telephone contacts. In Section 9.5 (Screen and baseline failures), "Influenza disease severity risk data" was removed as such data is not entered into the eCRF for this study. Edits have been made to the footnotes of study procedure (Table 2 and Table 3) for clarification purposes. The GSK Asset Number for the monovalent H5N1 vaccine was corrected. Minor editorial changes have also been made. |

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| 19 June 2012 | <p>At the European Medicines Agency's (EMA) request, GSK Biologicals has updated its procedure for emergency unblinding during the conduct of a clinical study. According to the revised procedure, the responsibility and the decision to break the treatment code in emergency situations resides solely with the investigator and consequently, the investigator will have full authority to break the treatment code.</p> <p>Clarification that unblinding at the subject level for site personnel, families, and monitors will occur after completion of RDE for all subjects, following their Day 385 contacts, rather than a batch of subjects at a time.</p> <p>In addition, a minor editorial error has been corrected.</p> |
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported