



Clinical trial results:

A phase II, double-blind, multicenter, randomized study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza candidate vaccine GSK2321138A compared with GSK Biologicals' trivalent influenza vaccine, Fluarix™, administered intramuscularly in children (18-47 months of age) in both unprimed subjects and in primed subjects who previously participated in the 111751 study

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2012-002587-27 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 21 May 2010 |

Results information

| | |
|--------------------------------|---|
| Result version number | v2 |
| This version publication date | 22 May 2016 |
| First version publication date | 15 July 2015 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Data correction due to a system error in EudraCT – Results (Primary endpoint) Data (typos) were corrected for 1 secondary endpoint |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 113237 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00985790 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | GlaxoSmithKline Biologicals |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330 |
| Public contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact | Clinical Trials 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 | 13 September 2010 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 21 May 2010 |
| Global end of trial reached? | Yes |
| Global end of trial date | 21 May 2010 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

- To assess the immunological non-inferiority in terms of Geometric Mean Titers (GMTs) of the quadrivalent influenza study vaccine (FLU D-QIV) compared to the trivalent influenza vaccine (Fluarix™) in primed and unprimed subjects for the three recommended seasonal strains, 28 days after the last vaccination.

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 | 08 October 2009 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Mexico: 599 |
| Worldwide total number of subjects | 599 |
| 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 | 299 |

| | |
|---------------------------|-----|
| months) | |
| Children (2-11 years) | 300 |
| 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:

A total of 599 subjects were enrolled in the study, and assigned to either the GSK2321138A Group (298 subjects) or the Fluarix Group (301 subjects). Duration of study was of approximately 6 months for each subject.

Pre-assignment

Screening details:

For demography and safety, results are presented as per the main study groups. For some outcome measures and where relevant, subjects as in these 2 main groups are split according to their priming status at study entry.

Period 1

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

Arms

| | |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | GSK2321138A Group |

Arm description:

Subjects aged between 18 and 47 months received the GSK2321138A. "Primed" subjects (subjects who had received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790 – or the GSK2321138A-Primed Group) received 1 dose of GSK2321138A vaccine at Day 0. "Unprimed" subject (subjects who had not received any 2-dose priming influenza immunization in any previous year – or the the GSK2321138A-Unprimed Group) received 2 doses of GSK2321138A vaccine at Days 0 and 28. The GSK2321138A vaccine was administered intramuscularly in the deltoid of the right arm.

| | |
|--|--------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | FLU D-QIV |
| Investigational medicinal product code | GSK2321138A |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

The vaccines were given intramuscularly in the deltoid of the right arm

| | |
|------------------|---------------|
| Arm title | Fluarix Group |
|------------------|---------------|

Arm description:

Subjects aged between 18 and 47 months received the Fluarix™ vaccine. "Primed" subjects (subjects who had received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790 – or the Fluarix-Primed Group) received 1 dose of Fluarix™ vaccine at Day 0. "Unprimed" subject (subjects who had not received any 2-dose priming influenza immunization in any previous year – or the the Fluarix-Unprimed Group) received 2 doses of Fluarix™ vaccine at Days 0 and 28. The Fluarix™ vaccine was administered intramuscularly in the deltoid of the right arm.

| | |
|--|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Fluarix™ |
| Investigational medicinal product code | |
| Other name | Trivalent Inactivated Influenza Vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

The Fluarix™ vaccine was administered intramuscularly in the deltoid of the right arm.

| Number of subjects in period 1 | GSK2321138A Group | Fluarix Group |
|---------------------------------------|----------------------|---------------|
| Started | 298 | 301 |
| Completed | 291 | 293 |
| Not completed | 7 | 8 |
| Consent withdrawn by subject | 1 | 1 |
| Lost to follow-up | 6 | 7 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | GSK2321138A Group |
|-----------------------|-------------------|

Reporting group description:

Subjects aged between 18 and 47 months received the GSK2321138A. "Primed" subjects (subjects who had received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790 – or the GSK2321138A-Primed Group) received 1 dose of GSK2321138A vaccine at Day 0. "Unprimed" subject (subjects who had not received any 2-dose priming influenza immunization in any previous year – or the the GSK2321138A-Unprimed Group) received 2 doses of GSK2321138A vaccine at Days 0 and 28. The GSK2321138A vaccine was administered intramuscularly in the deltoid of the right arm.

| | |
|-----------------------|---------------|
| Reporting group title | Fluarix Group |
|-----------------------|---------------|

Reporting group description:

Subjects aged between 18 and 47 months received the Fluarix™ vaccine. "Primed" subjects (subjects who had received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790 – or the Fluarix-Primed Group) received 1 dose of Fluarix™ vaccine at Day 0. "Unprimed" subject (subjects who had not received any 2-dose priming influenza immunization in any previous year – or the the Fluarix-Unprimed Group) received 2 doses of Fluarix™ vaccine at Days 0 and 28. The Fluarix™ vaccine was administered intramuscularly in the deltoid of the right arm.

| Reporting group values | GSK2321138A Group | Fluarix Group | Total |
|--|-------------------|---------------|-------|
| Number of subjects | 298 | 301 | 599 |
| Age categorical Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 0 |
| Newborns (0-27 days) | | | 0 |
| Infants and toddlers (28 days-23 months) | | | 0 |
| Children (2-11 years) | | | 0 |
| Adolescents (12-17 years) | | | 0 |
| Adults (18-64 years) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous Units: months | | | |
| arithmetic mean | 31.4 | 31.6 | |
| standard deviation | ± 8.46 | ± 8.29 | - |
| Gender categorical Units: Subjects | | | |
| Female | 138 | 147 | 285 |
| Male | 160 | 154 | 314 |

End points

End points reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | GSK2321138A Group |
|-----------------------|-------------------|

Reporting group description:

Subjects aged between 18 and 47 months received the GSK2321138A. "Primed" subjects (subjects who had received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790 – or the GSK2321138A-Primed Group) received 1 dose of GSK2321138A vaccine at Day 0. "Unprimed" subject (subjects who had not received any 2-dose priming influenza immunization in any previous year – or the the GSK2321138A-Unprimed Group) received 2 doses of GSK2321138A vaccine at Days 0 and 28. The GSK2321138A vaccine was administered intramuscularly in the deltoid of the right arm.

| | |
|-----------------------|---------------|
| Reporting group title | Fluarix Group |
|-----------------------|---------------|

Reporting group description:

Subjects aged between 18 and 47 months received the Fluarix™ vaccine. "Primed" subjects (subjects who had received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790 – or the Fluarix-Primed Group) received 1 dose of Fluarix™ vaccine at Day 0. "Unprimed" subject (subjects who had not received any 2-dose priming influenza immunization in any previous year – or the the Fluarix-Unprimed Group) received 2 doses of Fluarix™ vaccine at Days 0 and 28. The Fluarix™ vaccine was administered intramuscularly in the deltoid of the right arm.

| | |
|----------------------------|--------------------------|
| Subject analysis set title | GSK2321138A-Primed Group |
|----------------------------|--------------------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Subjects in this group were the primed subjects from the GSK2321138A Group, aged between 18 and 47 months, who received 1 dose of GSK2321138A vaccine at Day 0, and who had previously received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790. The GSK2321138A vaccine was administered intramuscularly in the deltoid of the right arm.

| | |
|----------------------------|----------------------------|
| Subject analysis set title | GSK2321138A-Unprimed Group |
|----------------------------|----------------------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Subjects in this group were the unprimed subjects from the GSK2321138A Group, aged between 18 and 47 months, who received 2 doses of GSK2321138A vaccine at Days 0 and 28, and who had not received any 2-dose priming influenza immunization in any previous year. The GSK2321138A vaccine was administered intramuscularly in the deltoid of the right arm.

| | |
|----------------------------|----------------------|
| Subject analysis set title | Fluarix-Primed Group |
|----------------------------|----------------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Subjects in this group were the primed subjects from the Fluarix Group, aged between 18 and 47 months, who received 1 dose of Fluarix™ vaccine at Day 0, and who had previously received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790. The Fluarix™ vaccine was administered intramuscularly in the deltoid of the right arm.

| | |
|----------------------------|------------------------|
| Subject analysis set title | Fluarix-Unprimed Group |
|----------------------------|------------------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Subjects in this group were the unprimed subjects from the Fluarix Group, aged between 18 and 47 months, who received 2 doses of Fluarix™ vaccine at Days 0 and 28, and who had not received any 2-dose priming influenza immunization in any previous year. The Fluarix™ vaccine was administered intramuscularly in the deltoid of the right arm.

Primary: Titers for serum Hemagglutination Inhibition (HI) antibodies against the 3 Fluarix vaccine strains.

| | |
|-----------------|---|
| End point title | Titers for serum Hemagglutination Inhibition (HI) antibodies against the 3 Fluarix vaccine strains. |
|-----------------|---|

End point description:

Titers are presented as geometric mean titers (GMTs). The reference cut-off value was 1:10. The 3 influenza strains assessed were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2) and Flu B/Brisbane/60/08 Victoria (VICT). The POST results were the primary outcome variables.

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

End point timeframe:

At Day 0 [PRE] and at 28 days post last vaccination (Day 28 or Day 56) [POST]

| End point values | GSK2321138A Group | Fluarix Group | | |
|--|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 193 | 193 | | |
| Units: titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H1N1, PRE [N=189;192] | 22.2 (17.2 to 28.7) | 21.6 (16.7 to 28) | | |
| H1N1, POST [N=193;193] | 173.8 (141.4 to 213.5) | 176.9 (143.3 to 218.5) | | |
| H3N2, PRE [N=190;192] | 18.6 (14.9 to 23.2) | 20.8 (16.5 to 26.2) | | |
| H3N2, POST [N=193;193] | 120.7 (101.2 to 143.9) | 130.4 (108 to 157.5) | | |
| VICT, PRE [N=190;192] | 8.7 (7.3 to 10.2) | 9 (7.7 to 10.6) | | |
| VICT, POST [N=192;193] | 61.9 (48.7 to 78.6) | 66.6 (52.4 to 84.7) | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Adjusted GMT ratio for FLU A/Bri/59/07 H1N1 |
| Statistical analysis description: To assess the immunological non-inferiority in terms of Geometric Mean Titers (GMTs) of the GSK2321138A vaccine compared to the Fluarix vaccine in primed and unprimed subjects for the three recommended seasonal strains, 28 days after the last vaccination. | |
| Comparison groups | GSK2321138A Group v Fluarix Group |
| Number of subjects included in analysis | 386 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[1] |
| Parameter estimate | Adjusted GMT ratio |
| Point estimate | 1.05 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.84 |
| upper limit | 1.33 |

Notes:

[1] - Non-inferiority criterion: UL of the two-sided 95% CI on GMT ratio < 2.

| | |
|--|--|
| Statistical analysis title | Adjusted GMT ratio for Flu A/Uru/716/07 H3N2 |
| Statistical analysis description: To assess the immunological non-inferiority in terms of Geometric Mean Titers (GMTs) of the GSK2321138A vaccine compared to the Fluarix vaccine in primed and unprimed subjects for the three recommended seasonal strains, 28 days after the last vaccination. | |
| Comparison groups | GSK2321138A Group v Fluarix Group |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 386 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[2] |
| Parameter estimate | Adjusted GMT ratio |
| Point estimate | 1.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.85 |
| upper limit | 1.23 |

Notes:

[2] - Non-inferiority criterion: UL of the two-sided 95% CI on GMT ratio < 2.

| | |
|-----------------------------------|--|
| Statistical analysis title | Adjusted GMT ratio for FluB/Bri/60/08 Victoria |
|-----------------------------------|--|

Statistical analysis description:

To assess the immunological non-inferiority in terms of Geometric Mean Titers (GMTs) of the GSK2321138A vaccine compared to the Fluarix vaccine in primed and unprimed subjects for the three recommended seasonal strains, 28 days after the last vaccination.

| | |
|---|-----------------------------------|
| Comparison groups | GSK2321138A Group v Fluarix Group |
| Number of subjects included in analysis | 386 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[3] |
| Parameter estimate | Adjusted GMT ratio |
| Point estimate | 1.05 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.81 |
| upper limit | 1.37 |

Notes:

[3] - Non-inferiority criterion: UL of the two-sided 95% CI on GMT ratio < 2.

Secondary: Titers for serum Hemagglutination Inhibition (HI) antibodies against 4 strains of influenza disease.

| | |
|-----------------|--|
| End point title | Titers for serum Hemagglutination Inhibition (HI) antibodies against 4 strains of influenza disease. |
|-----------------|--|

End point description:

Titers are presented as geometric mean titers (GMTs). The reference cut-off value was 1:10. The 4 influenza strains assessed were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the primed groups.

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

End point timeframe:

At Days 0 and 28.

| End point values | GSK2321138A- Primed Group | Fluarix-Primed Group | | |
|---|------------------------------|---------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 94 | 95 | | |
| Units: titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H1N1, Day 0 | 40.3 (27 to 60.2) | 36.5 (24.3 to 54.9) | | |
| H1N1, Day 28 | 117 (83.2 to 164.5) | 124.4 (89.8 to 172.4) | | |
| H3N2, Day 0 | 22.8 (16.7 to 31.2) | 21.7 (16 to 29.5) | | |
| H3N2, Day 28 | 85.2 (64.8 to 112) | 83 (63.6 to 108.2) | | |
| VICT, Day 0 | 8.9 (7.2 to 11) | 9.7 (7.7 to 12.4) | | |
| VICT, Day 28 | 38.7 (26.2 to 57.1) | 44 (29.6 to 65.2) | | |
| YAMA, Day 0 | 29.3 (23 to 37.4) | 37.7 (29.8 to 47.8) | | |
| YAMA, Day 28 | 243.6 (198.1 to 299.6) | 127.2 (106.1 to 152.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for serum Hemagglutination Inhibition (HI) antibodies against 4 strains of influenza disease.

| | |
|-----------------|--|
| End point title | Titers for serum Hemagglutination Inhibition (HI) antibodies against 4 strains of influenza disease. |
|-----------------|--|

End point description:

Titers are presented as geometric mean titers (GMTs). The reference cut-off value was 1:10. The 4 influenza strains assessed were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the unprimed groups.

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

End point timeframe:

At Days 0, 28 and Day 56

| End point values | GSK2321138A- Unprimed Group | Fluarix- Unprimed Group | | |
|---|-----------------------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 192 | 198 | | |
| Units: titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H1N1, Day 0 [N=190;198] | 14.7 (11.8 to 18.4) | 12.8 (10.5 to 15.7) | | |
| H1N1, Day 28 [N=97;101] | 173.1 (113.1 to 264.8) | 161.6 (103.9 to 251.4) | | |

| | | | | |
|-------------------------|------------------------|------------------------|--|--|
| H1N1, Day 56 [N=99;98] | 253.1 (203.4 to 314.8) | 249 (192.5 to 321.9) | | |
| H3N2, Day 0 [N=192;197] | 17.7 (14.1 to 22.1) | 17.9 (14.1 to 22.6) | | |
| H3N2, Day 28 [N=96;101] | 99.3 (64.8 to 152.2) | 84.2 (54.1 to 131.2) | | |
| H3N2, Day 56 [N=99;98] | 168.1 (136.6 to 206.7) | 202.1 (158.6 to 257.5) | | |
| VICT, Day 0 [N=190;198] | 7.8 (6.7 to 9.2) | 8.7 (7.5 to 10.3) | | |
| VICT, Day 28 [N=95;101] | 26.5 (17.7 to 39.7) | 34.6 (22.4 to 53.6) | | |
| VICT, Day 56 [N=98;98] | 97.2 (74.9 to 126.1) | 99.6 (76.7 to 129.4) | | |
| YAMA, Day 0 [N=188;198] | 9.1 (7.7 to 10.7) | 9.9 (8.4 to 11.8) | | |
| YAMA, Day 28 [N=97;102] | 97 (64.7 to 145.4) | 30 (21.3 to 42.1) | | |
| YAMA, Day 56 [N=99;98] | 311.1 (255.4 to 379.1) | 42.2 (30.6 to 58.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects against 4 strains of influenza disease.

| | |
|--|---|
| End point title | Number of seropositive subjects against 4 strains of influenza disease. |
| End point description: | |
| A seropositive subject was defined as a vaccinated subject with serum Hemagglutination Inhibition (HI) titer $\geq 1:10$. The 4 assessed influenza strains were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the primed groups. | |
| End point type | Secondary |
| End point timeframe: | |
| At Days 0 and 28 | |

| End point values | GSK2321138A-Primed Group | Fluarix-Primed Group | | |
|-----------------------------|--------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 94 | 95 | | |
| Units: Subjects | | | | |
| H1N1, Day 0 | 58 | 54 | | |
| H1N1, Day 28 | 83 | 87 | | |
| H3N2, Day 0 | 60 | 59 | | |
| H3N2, Day 28 | 88 | 87 | | |
| VICT, Day 0 | 26 | 28 | | |
| VICT, Day 28 | 62 | 66 | | |
| YAMA, Day 0 | 73 | 80 | | |
| YAMA, Day 28 | 93 | 94 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects against 4 strains of influenza disease.

| | |
|-----------------|---|
| End point title | Number of seropositive subjects against 4 strains of influenza disease. |
|-----------------|---|

End point description:

A seropositive subject was defined as a vaccinated subject with serum Hemagglutination Inhibition (HI) titer $\geq 1:10$. The 4 assessed influenza strains were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the unprimed groups.

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

End point timeframe:

At Days 0, 28 and 56

| End point values | GSK2321138A- Unprimed Group | Fluarix- Unprimed Group | | |
|-----------------------------|-----------------------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 192 | 198 | | |
| Units: Subjects | | | | |
| H1N1, Day 0 [N=190;198] | 75 | 71 | | |
| H1N1, Day 28 [N=97;101] | 83 | 84 | | |
| H1N1, Day 56 [N=99;98] | 99 | 96 | | |
| H3N2, Day 0 [N=192;197] | 85 | 82 | | |
| H3N2, Day 28 [N=96;101] | 74 | 78 | | |
| H3N2, Day 56 [N=99;98] | 99 | 98 | | |
| VICT, Day 0 [N=190; 198] | 30 | 42 | | |
| VICT, Day 28 [N=95; 101] | 51 | 61 | | |
| VICT, Day 56 [N=98; 98] | 96 | 94 | | |
| YAMA, Day 0 [N=188;198] | 45 | 57 | | |
| YAMA, Day 28 [N=97;102] | 75 | 57 | | |
| YAMA, Day 56 [N=99;98] | 98 | 70 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects against 4 strains of influenza disease.

| | |
|-----------------|--|
| End point title | Number of seroconverted subjects against 4 strains of influenza disease. |
|-----------------|--|

End point description:

A seroconverted subject was defined as a vaccinated subject who had either a pre-vaccination titer <1:10 and a post-vaccination titer \geq 1:40 or a pre-vaccination titer \geq 1:10 and at least a four-fold increase in post-vaccination titer. The 4 assessed influenza strains were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the primed groups.

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

End point timeframe:

At Day 28

| End point values | GSK2321138A- Primed Group | Fluarix-Primed Group | | |
|-----------------------------|------------------------------|-------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 94 | 95 | | |
| Units: Subjects | | | | |
| H1N1, Day 28 | 30 | 39 | | |
| H3N2, Day 28 | 48 | 46 | | |
| VICT, Day 28 | 46 | 42 | | |
| YAMA, Day 28 | 82 | 40 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects against 4 strains of influenza disease.

| | |
|-----------------|--|
| End point title | Number of seroconverted subjects against 4 strains of influenza disease. |
|-----------------|--|

End point description:

A seroconverted subject was defined as a vaccinated subject who had either a pre-vaccination titer <1:10 and a post-vaccination titer \geq 1:40 or a pre-vaccination titer \geq 1:10 and at least a four-fold increase in post-vaccination titer. The 4 assessed influenza strains were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the unprimed groups.

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

End point timeframe:

At Days 28 and 56

| End point values | GSK2321138A- Unprimed Group | Fluarix- Unprimed Group | | |
|-----------------------------|-----------------------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 96 | 101 | | |
| Units: Subjects | | | | |
| H1N1, Day 28 [N=95;101] | 63 | 74 | | |
| H1N1, Day 56 [N=95;97] | 81 | 89 | | |
| H3N2, Day 28 [N=96;100] | 55 | 54 | | |
| H3N2, Day 56 [N=96;97] | 79 | 75 | | |

| | | | | |
|-------------------------|----|----|--|--|
| VICT, Day 28 [N=94;101] | 34 | 40 | | |
| VICT, Day 56 [N=95;97] | 77 | 85 | | |
| YAMA, Day 28 [N=93;101] | 59 | 40 | | |
| YAMA, Day 56 [N=95;97] | 90 | 42 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Seroconversion factor for Hemagglutination Inhibition (HI) antibodies against 4 strains of influenza disease.

| | |
|-----------------|---|
| End point title | Seroconversion factor for Hemagglutination Inhibition (HI) antibodies against 4 strains of influenza disease. |
|-----------------|---|

End point description:

The seroconversion factor (SCF) was defined as the fold increase in serum Hemagglutination Inhibition (HI) geometric mean titers (GMTs) post vaccination compared to Day 0. The 4 assessed influenza strains were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the primed groups.

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

End point timeframe:

At Day 28

| End point values | GSK2321138A-Primed Group | Fluarix-Primed Group | | |
|--|--------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 94 | 95 | | |
| Units: fold increase | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H1N1, Day 28 | 2.9 (2.3 to 3.6) | 3.4 (2.7 to 4.2) | | |
| H3N2, Day 28 | 3.7 (3.1 to 4.5) | 3.8 (3.1 to 4.7) | | |
| VICT, Day 28 | 4.4 (3.3 to 5.8) | 4.5 (3.4 to 6) | | |
| YAMA, Day 28 | 8.3 (6.8 to 10.1) | 3.4 (2.8 to 4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Seroconversion factor for Hemagglutination Inhibition (HI) antibodies against 4 strains of influenza disease.

| | |
|-----------------|---|
| End point title | Seroconversion factor for Hemagglutination Inhibition (HI) antibodies against 4 strains of influenza disease. |
|-----------------|---|

End point description:

The seroconversion factor (SCF) was defined as the fold increase in serum Hemagglutination Inhibition (HI) geometric mean titers (GMTs) post vaccination compared to Day 0. The 4 assessed influenza

strains were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the unprimed groups.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At Days 28 and 56 | |

| End point values | GSK2321138A- Unprimed Group | Fluarix- Unprimed Group | | |
|--|-----------------------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 96 | 101 | | |
| Units: fold increase | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H1N1, Day 28 [N=95;101] | 9.9 (7 to 14.1) | 12.7 (9.1 to 17.7) | | |
| H1N1, Day 56 [N=95;97] | 19.8 (15.4 to 25.6) | 19.2 (15.2 to 24.2) | | |
| H3N2, Day 28 [N=96;100] | 4.9 (3.7 to 6.3) | 5.1 (3.9 to 6.7) | | |
| H3N2, Day 56 [N=96;97] | 11.1 (9 to 13.7) | 10.3 (8.3 to 12.9) | | |
| VICT, Day 28 [N=94;101] | 3.6 (2.7 to 5) | 3.8 (2.9 to 5) | | |
| VICT, Day 56 [N=95;97] | 11.3 (9.4 to 13.6) | 12.1 (9.8 to 14.8) | | |
| YAMA, Day 28 [N=93;101] | 9.9 (6.9 to 14) | 3.4 (2.5 to 4.5) | | |
| YAMA, Day 56 [N=95;97] | 35.1 (27.6 to 44.6) | 3.7 (2.9 to 4.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects against 4 strains of influenza disease.

| | |
|-----------------|--|
| End point title | Number of seroprotected subjects against 4 strains of influenza disease. |
|-----------------|--|

End point description:

A seroprotected subject was defined as a vaccinated subject with serum Hemagglutination Inhibition (HI) titer $\geq 1:40$. The 4 assessed influenza strains were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the primed groups.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At Days 0 and 28 | |

| End point values | GSK2321138A- Primed Group | Fluarix-Primed Group | | |
|-----------------------------|------------------------------|-------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 94 | 95 | | |
| Units: Subjects | | | | |
| H1N1, Day 0 | 48 | 45 | | |
| H1N1, Day 28 | 73 | 78 | | |
| H3N2, Day 0 | 39 | 36 | | |
| H3N2, Day 28 | 75 | 80 | | |
| VICT, Day 0 | 16 | 20 | | |
| VICT, Day 28 | 50 | 52 | | |
| YAMA, Day 0 | 56 | 62 | | |
| YAMA, Day 28 | 91 | 90 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects against 4 strains of influenza disease.

| | |
|---|--|
| End point title | Number of seroprotected subjects against 4 strains of influenza disease. |
| End point description: | |
| A seroprotected subject was defined as a vaccinated subject with serum Hemagglutination Inhibition (HI) titer $\geq 1:40$. The 4 assessed influenza strains were the FLU A/Brisbane/59/07 (H1N1), Flu A/Uruguay/716/07 (H3N2), Flu B/Brisbane/60/08 Victoria (VICT) and Flu B/Brisbane/3/07 Yamagata (YAMA). This outcome only covers the results for the unprimed groups. | |
| End point type | Secondary |
| End point timeframe: | |
| At Days 0, 28 and 56 | |

| End point values | GSK2321138A- Unprimed Group | Fluarix- Unprimed Group | | |
|-----------------------------|-----------------------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 192 | 198 | | |
| Units: Subjects | | | | |
| H1N1, Day 0 [N=190;198] | 58 | 54 | | |
| H1N1, Day 28 [N=97;101] | 76 | 78 | | |
| H1N1, Day 56 [N=99;98] | 95 | 94 | | |
| H3N2, Day 0 [N=192;197] | 74 | 70 | | |
| H3N2, Day 28 [N=96;101] | 64 | 61 | | |
| H3N2, Day 56 [N=99;98] | 96 | 94 | | |
| VICT, Day 0 [N=190;198] | 25 | 35 | | |
| VICT, Day 28 [N=95;101] | 36 | 41 | | |
| VICT, Day 56 [N=98;98] | 84 | 88 | | |
| YAMA, Day 0 [N=188;198] | 37 | 40 | | |
| YAMA, Day 28 [N=97;102] | 67 | 53 | | |
| YAMA, Day 56 [N=99;98] | 98 | 59 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and grade 3 solicited local symptoms.

| | |
|-----------------|---|
| End point title | Number of subjects with any and grade 3 solicited local symptoms. |
|-----------------|---|

End point description:

Assessed solicited local symptoms were pain, redness and swelling at the injection site. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 50 millimeters (mm) of injection site.

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

End point timeframe:

During the 7-day follow-up period (Days 0 to 6) after any vaccination

| End point values | GSK2321138A Group | Fluarix Group | | |
|-----------------------------|-------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 293 | 298 | | |
| Units: Subjects | | | | |
| Any Pain | 125 | 116 | | |
| Grade 3 Pain | 4 | 1 | | |
| Any Redness | 31 | 34 | | |
| Redness >50 mm | 0 | 0 | | |
| Any Swelling | 27 | 24 | | |
| Swelling >50 mm | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and related solicited general symptoms.

| | |
|-----------------|--|
| End point title | Number of subjects with any, grade 3 and related solicited general symptoms. |
|-----------------|--|

End point description:

Assessed solicited general symptoms were drowsiness, irritability, loss of appetite and temperature (defined as axillary temperature equal to or above 37.5 degrees Celsius). For other symptoms: Any = any solicited general symptom reported irrespective of intensity and relationship to vaccination. Related = symptoms assessed by the investigator as related to vaccination. Grade 3 drowsiness = prevented normal activity. Grade 3 loss of appetite = not eating at all. Grade 3 irritability= crying that could not be comforted/prevented normal activity. Grade 3 temperature: $\geq 39.0^{\circ}\text{C}$.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| During the 7-day follow-up period (Days 0 to 6) after any vaccination | |

| End point values | GSK2321138A Group | Fluarix Group | | |
|---|-------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 293 | 298 | | |
| Units: Subjects | | | | |
| Any Drowsiness | 70 | 62 | | |
| Grade 3 Drowsiness | 2 | 0 | | |
| Related Drowsiness | 64 | 57 | | |
| Any Irritability | 90 | 87 | | |
| Grade 3 Irritability | 4 | 2 | | |
| Related Irritability | 83 | 78 | | |
| Any Loss of appetite | 89 | 86 | | |
| Grade 3 Loss of appetite | 4 | 3 | | |
| Related Loss of appetite | 79 | 68 | | |
| Temperature $\geq 37.5^{\circ}\text{C}$ | 74 | 79 | | |
| Temperature $> 39.0^{\circ}\text{C}$ | 3 | 3 | | |
| Related Temperature | 63 | 62 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and related unsolicited adverse events (AEs).

| | |
|-----------------|--|
| End point title | Number of subjects with any, grade 3 and related unsolicited adverse events (AEs). |
|-----------------|--|

End point description:

An unsolicited AE covers any untoward medical occurrence in a subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and 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 = occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. Grade 3 = an AE which prevented normal, everyday activities. Related = AE assessed by the investigator as related to vaccination.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| During the 28-day follow-up period (Days 0 to 27) after vaccination | |

| | | | | |
|-----------------------------|-------------------|-----------------|--|--|
| End point values | GSK2321138A Group | Fluarix Group | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 298 | 301 | | |
| Units: Subjects | | | | |
| Subjects with any AE(s) | 116 | 118 | | |
| Subjects with Grade 3 AE(s) | 10 | 12 | | |
| Subjects with related AE(s) | 7 | 9 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and related serious adverse events (SAEs).

| | |
|-----------------|--|
| End point title | Number of subjects with any and related serious adverse events (SAEs). |
|-----------------|--|

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity. Any was defined as occurrence of any symptom regardless of intensity grade 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 to Day 180 (study conclusion)

| | | | | |
|-----------------------------|-------------------|-----------------|--|--|
| End point values | GSK2321138A Group | Fluarix Group | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 298 | 301 | | |
| Units: Subjects | | | | |
| Any SAE(s) | 0 | 2 | | |
| Related SAE(s) | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any adverse events of specific interest (AESIs).

| | |
|-----------------|--|
| End point title | Number of subjects with any adverse events of specific interest (AESIs). |
|-----------------|--|

End point description:

An AESI was defined as an AE including autoimmune diseases and other mediated inflammatory disorders and assessed by the investigator as specific to the treatment administration.

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

End point timeframe:

From Day 0 to Day 180 (study conclusion)

| End point values | GSK2321138A Group | Fluarix Group | | |
|-----------------------------|-------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 298 | 301 | | |
| Units: Subjects | | | | |
| Subjects with any AESI(s) | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAE(s): during the entire study period (Day 0 - Day 180); Unsolicited AE(s): during the 28-day follow-up period (Days 0 to 27) after any vaccination; Solicited local and general symptoms: during the 7-day (Days 0-6) follow-up period after any vaccination.

Adverse event reporting additional description:

The number of occurrences reported for solicited symptoms, adverse events, and serious adverse events were not available for posting. The number of subjects affected by each specific event was indicated as the number of occurrences.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 13.0 |

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | Fluarix Group |
|-----------------------|---------------|

Reporting group description:

Subjects aged between 18 and 47 months received the Fluarix™ vaccine. "Primed" subjects (subjects who had received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790 – or the Fluarix-Primed Group) received 1 dose of Fluarix™ vaccine at Day 0. "Unprimed" subject (subjects who had not received any 2-dose priming influenza immunization in any previous year – or the Fluarix-Unprimed Group) received 2 doses of Fluarix™ vaccine at Days 0 and 28. The Fluarix™ vaccine was administered intramuscularly in the deltoid of the right arm.

| | |
|-----------------------|-------------------|
| Reporting group title | GSK2321138A Group |
|-----------------------|-------------------|

Reporting group description:

Subjects aged between 18 and 47 months received the GSK2321138A. "Primed" subjects (subjects who had received a 2-dose priming immunization with Fluarix™ vaccine in study NCT00764790 – or the GSK2321138A-Primed Group) received 1 dose of GSK2321138A vaccine at Day 0. "Unprimed" subject (subjects who had not received any 2-dose priming influenza immunization in any previous year – or the GSK2321138A-Unprimed Group) received 2 doses of GSK2321138A vaccine at Days 0 and 28. The GSK2321138A vaccine was administered intramuscularly in the deltoid of the right arm.

| Serious adverse events | Fluarix Group | GSK2321138A Group | |
|---|-----------------|-------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 301 (0.66%) | 0 / 298 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Urticaria | | | |
| subjects affected / exposed | 1 / 301 (0.33%) | 0 / 298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Bronchopneumonia | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 301 (0.33%) | 0 / 298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Fluarix Group | GSK2321138A Group | |
|---|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 116 / 301 (38.54%) | 125 / 298 (41.95%) | |
| General disorders and administration site conditions | | | |
| Drowsiness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[1] | 62 / 298 (20.81%) | 70 / 293 (23.89%) | |
| occurrences (all) | 62 | 70 | |
| Irritability | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[2] | 87 / 298 (29.19%) | 90 / 293 (30.72%) | |
| occurrences (all) | 87 | 90 | |
| Loss of appetite | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[3] | 86 / 298 (28.86%) | 89 / 293 (30.38%) | |
| occurrences (all) | 86 | 89 | |
| Temperature | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[4] | 79 / 298 (26.51%) | 74 / 293 (25.26%) | |
| occurrences (all) | 79 | 74 | |
| Pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[5] | 116 / 298 (38.93%) | 125 / 293 (42.66%) | |
| occurrences (all) | 116 | 125 | |
| Redness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[6] | 34 / 298 (11.41%) | 31 / 293 (10.58%) | |
| occurrences (all) | 34 | 31 | |

| | | | |
|---|---|---|--|
| Swelling alternative assessment type: Systematic subjects affected / exposed ^[7] occurrences (all) | 24 / 298 (8.05%) 24 | 27 / 293 (9.22%) 27 | |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Pharyngitis subjects affected / exposed occurrences (all) | 69 / 301 (22.92%) 69 21 / 301 (6.98%) 21 | 72 / 298 (24.16%) 72 20 / 298 (6.71%) 20 | |

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.

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).

[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.

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).

[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.

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).

[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.

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).

[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.

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).

[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.

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? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported