



Clinical trial results:

A Phase IV, open label, randomized, monocentric study to evaluate immunogenicity and safety of GSK Biologicals' seasonal (2010-2011) influenza vaccine FluarixTM in adolescents previously vaccinated with GSK Biologicals' H1N1 vaccine (PandemrixTM).

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2010-020331-39 |
| Trial protocol | FI |
| Global end of trial date | 07 July 2011 |

Results information

| | |
|--------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Result version number | v2 |
| This version publication date | 05 May 2016 |
| First version publication date | 07 March 2015 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Data (typos) were corrected in Protection of trial subjects section and some of the endpoints. |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 114452 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01190215 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--------------------------------------------------------------------------------------------------------|
| Sponsor organisation name | GlaxoSmithKline Biologicals |
| Sponsor organisation address | Rue Fleming 20, Wavre, Belgium, 1300 |
| Public contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 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 September 2011 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 07 July 2011 |
| Global end of trial reached? | Yes |
| Global end of trial date | 07 July 2011 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate HI immune response against the H1N1 strain 28 days following vaccination with TIV vaccine (Fluarix) in subjects previously vaccinated with 1 dose of H1N1 adjuvanted vaccine (Pandemrix) in the TIV Group.

Protection of trial subjects:

All subjects were supervised for 30 min after vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Only eligible subjects that had no contraindications to any components of the vaccines were vaccinated. Subjects were followed-up until Month 6 after each/last vaccination.

Background therapy: -

Evidence for comparator: -

| | |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment | 21 December 2010 |
| 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 | Finland: 77 |
| Worldwide total number of subjects | 77 |
| EEA total number of subjects | 77 |

Notes:

Subjects enrolled per age group

| | |
|-------------------------------------------|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 77 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | Up to Day 28 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

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

Arm description:

Subjects previously vaccinated with Pandemrix vaccine received 1 dose of Fluarix vaccine. All vaccines were administered in the deltoid region of the non-dominant arm on Day 0.

| | |
|----------------------------------------|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Biological: Fluarix TM |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

One Intramuscular injection

| | |
|------------------|--------------|
| Arm title | Havrix Group |
|------------------|--------------|

Arm description:

Subjects previously vaccinated with Pandemrix vaccine received 1 first dose of Havrix vaccine (subjects aged above 15 years) or Havrix-Junior vaccine (subjects aged 15 years and below). A second dose was given outside the study setting, at Month 6. All vaccines were administered in the deltoid region of the non-dominant arm on Day 0.

| | |
|----------------------------------------|-----------------------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Biological: Havrix TM Junior |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Two Intramuscular injections

| Number of subjects in period 1 | Fluarix Group | Havrix Group |
|--------------------------------|---------------|--------------|
| Started | 38 | 39 |
| Completed | 38 | 39 |

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | Up to Month 6 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

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

Arm description:

Subjects previously vaccinated with Pandemrix vaccine received 1 dose of Fluarix vaccine. All vaccines were administered in the deltoid region of the non-dominant arm on Day 0.

| | |
|----------------------------------------|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Biological: FluarixTM |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects previously vaccinated with Pandemrix vaccine received 1 dose of Fluarix vaccine. All vaccines were administered in the deltoid region of the non-dominant arm on Day 0.

| | |
|----------------------------------------|----------------------|
| Investigational medicinal product name | Biological: HavrixTM |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects previously vaccinated with Pandemrix vaccine received 1 first dose of Havrix vaccine (subjects aged above 15 years) or Havrix-Junior vaccine (subjects aged 15 years and below). A second dose was given outside the study setting, at Month 6. All vaccines were administered in the deltoid region of the non-dominant arm on Day 0.

| | |
|------------------|--------------|
| Arm title | Havrix Group |
|------------------|--------------|

Arm description:

Subjects previously vaccinated with Pandemrix vaccine received 1 first dose of Havrix vaccine (subjects aged above 15 years) or Havrix-Junior vaccine (subjects aged 15 years and below). A second dose was given outside the study setting, at Month 6. All vaccines were administered in the deltoid region of the non-dominant arm on Day 0.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|----------------------------------------|---------------------|
| Investigational medicinal product name | Biological: Havrix™ |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects previously vaccinated with Pandemrix vaccine received 1 first dose of Havrix vaccine (subjects aged above 15 years) or Havrix-Junior vaccine (subjects aged 15 years and below). A second dose was given outside the study setting, at Month 6. All vaccines were administered in the deltoid region of the non-dominant arm on Day 0.

| Number of subjects in period 2 | Fluarix Group | Havrix Group |
|---------------------------------------|---------------|--------------|
| Started | 38 | 39 |
| Completed | 36 | 39 |
| Not completed | 2 | 0 |
| Lost to follow-up | 2 | - |

Baseline characteristics

Reporting groups

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

Reporting group description:

Subjects previously vaccinated with Pandemrix vaccine received 1 dose of Fluarix vaccine. All vaccines were administered in the deltoid region of the non-dominant arm on Day 0.

| | |
|-----------------------|--------------|
| Reporting group title | Havrix Group |
|-----------------------|--------------|

Reporting group description:

Subjects previously vaccinated with Pandemrix vaccine received 1 first dose of Havrix vaccine (subjects aged above 15 years) or Havrix-Junior vaccine (subjects aged 15 years and below). A second dose was given outside the study setting, at Month 6. All vaccines were administered in the deltoid region of the non-dominant arm on Day 0.

| Reporting group values | Fluarix Group | Havrix Group | Total |
|-------------------------------------------------------|---------------|--------------|-------|
| Number of subjects | 38 | 39 | 77 |
| 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: years | | | |
| arithmetic mean | 14.6 | 14.7 | |
| standard deviation | ± 2.22 | ± 2.28 | - |
| Gender categorical Units: Subjects | | | |
| Female | 22 | 19 | 41 |
| Male | 16 | 20 | 36 |

End points

End points reporting groups

| | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|
| Reporting group title | Fluarix Group |
| Reporting group description: Subjects previously vaccinated with Pandemrix vaccine received 1 dose of Fluarix vaccine. All vaccines were administered in the deltoid region of the non-dominant arm on Day 0. | |
| Reporting group title | Havrix Group |
| Reporting group description: Subjects previously vaccinated with Pandemrix vaccine received 1 first dose of Havrix vaccine (subjects aged above 15 years) or Havrix-Junior vaccine (subjects aged 15 years and below). A second dose was given outside the study setting, at Month 6. All vaccines were administered in the deltoid region of the non-dominant arm on Day 0. | |
| Reporting group title | Fluarix Group |
| Reporting group description: Subjects previously vaccinated with Pandemrix vaccine received 1 dose of Fluarix vaccine. All vaccines were administered in the deltoid region of the non-dominant arm on Day 0. | |
| Reporting group title | Havrix Group |
| Reporting group description: Subjects previously vaccinated with Pandemrix vaccine received 1 first dose of Havrix vaccine (subjects aged above 15 years) or Havrix-Junior vaccine (subjects aged 15 years and below). A second dose was given outside the study setting, at Month 6. All vaccines were administered in the deltoid region of the non-dominant arm on Day 0. | |

Primary: Geometric mean antibody titres for haemagglutination inhibition (HI) antibodies against Fluarix vaccine containing H1N1 strain.

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Geometric mean antibody titres for haemagglutination inhibition (HI) antibodies against Fluarix vaccine containing H1N1 strain. ^[1] |
| End point description: Fluarix vaccine strain was Flu A/California/7/2009 (H1N1). Day 28 data were presented only for the Fluarix Group. Titres were expressed as geometric mean antibody titre. | |
| End point type | Primary |
| End point timeframe: At Day 0 and Day 28 | |

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 scope of this primary endpoint was descriptive, no statistical analyses were conducted.

| End point values | Fluarix Group | Havrix Group | | |
|------------------------------------------|------------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 33 | 39 | | |
| Units: Titres | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Flu A/Cal/7/09 H1N1 [Day 0] | 150.1 (105.8 to 213) | 150.3 (106 to 213.3) | | |
| Flu A/Cal/7/09 H1N1 [Day 28] | 646.8 (534.6 to 782.6) | 0 (0 to 0) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of seropositive subjects for haemagglutination inhibition (HI) antibodies against Fluarix vaccine containing H1N1 strain.

| | |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of seropositive subjects for haemagglutination inhibition (HI) antibodies against Fluarix vaccine containing H1N1 strain. ^[2] |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Fluarix vaccine strain was Flu A/California/7/2009 (H1N1). Seropositivity was assessed for subjects with an antibody titre assay cut-off value equal to or above 1:10. Day 28 data was presented only for the Fluarix Group.

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

End point timeframe:

At Day 0 and Day 28

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 scope of this primary endpoint was descriptive, no statistical analyses were conducted.

| End point values | Fluarix Group | Havrix Group | | |
|------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 33 | 39 | | |
| Units: Subjects | | | | |
| Flu A/Cal/7/09 H1N1 [Day 0] | 33 | 39 | | |
| Flu A/Cal/7/09 H1N1 [Day 28] | 33 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroconverted subjects for haemagglutination inhibition (HI) antibodies against Fluarix vaccine containing H1N1 strain.

| | |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of seroconverted subjects for haemagglutination inhibition (HI) antibodies against Fluarix vaccine containing H1N1 strain. ^{[3][4]} |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Fluarix vaccine strain was Flu A/California/7/2009 (H1N1). A seroconverted subject was a subject who had either a pre-vaccination (Day 0) titre less than ($<$) 1:10 and a post-vaccination titre greater than or equal to (\geq) 1:40 or a pre-vaccination titre \geq 1:10 and at least a 4-fold increase in post-vaccination titre. Day 28 data were presented for the Fluarix Group only.

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

End point timeframe:

At Day 28

Notes:

[3] - 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 scope of this primary endpoint was descriptive, no statistical analyses were conducted.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Day 28 data were presented for the Fluarix Group only.

| End point values | Fluarix Group | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 33 | | | |
| Units: Subjects | | | | |
| Flu A/California/7/2009 | 16 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects for haemagglutination inhibition (HI) antibodies against Fluarix vaccine containing H1N1 strain.

| | |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of seroprotected subjects for haemagglutination inhibition (HI) antibodies against Fluarix vaccine containing H1N1 strain. ^[5] |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Fluarix vaccine strain was Flu A/California/7/2009 (H1N1). A seroprotected subject was a subject with a serum HI titre $\geq 1:40$ that usually is accepted as indicating protection. Day 28 data were presented for the Fluarix Group only.

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

End point timeframe:

At Day 0 and Day 28

Notes:

[5] - 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 scope of this primary endpoint was descriptive, no statistical analyses were conducted.

| End point values | Fluarix Group | Havrix Group | | |
|------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 33 | 39 | | |
| Units: Subjects | | | | |
| Flu A/Cal/7/09 H1N1 [Day 0] | 31 | 36 | | |
| Flu A/Cal/7/09 H1N1 [Day 28] | 33 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Mean geometric increase (MG I) for haemagglutination inhibition (HI) antibodies against Fluarix vaccine containing H1N1 strain.

| | |
|-----------------|------------------------------------------------------|
| End point title | Mean geometric increase (MG I) for haemagglutination |
|-----------------|------------------------------------------------------|

End point description:

Fluarix vaccine strain was Flu A/California/7/2009 (H1N1). MGI is defined as the geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the pre-vaccination (Day 0) reciprocal HI titre. Day 28 data were presented for the Fluarix Group only.

End point type Primary

End point timeframe:

At Day 28

Notes:

[6] - 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 scope of this primary endpoint was descriptive, no statistical analyses were conducted.

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Day 28 data were presented for the Fluarix Group only.

| End point values | Fluarix Group | | | |
|------------------------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 33 | | | |
| Units: Ratio | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Flu A/Cal/7/09 H1N1 | 4.3 (2.9 to 6.4) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean antibody titres for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains.

End point title Geometric mean antibody titres for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains.

End point description:

Fluarix vaccine strains were Flu A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2) and B/Brisbane/60/2008. Day 28 data were presented for the Fluarix Group only. Titres were expressed as geometric mean antibody titres (GMTs). Only data for the Flu A/California/7/2009 (H1N1) strain were presented for the Havrix Group.

End point type Secondary

End point timeframe:

At Day 0 and Day 28

| End point values | Fluarix Group | Havrix Group | | |
|------------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 33 | 39 | | |
| Units: Titres | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Flu A/Cal/7/09 H1N1 [Day 0] | 150.1 (105.8 to 213) | 150.3 (106 to 213.3) | | |

| | | | | |
|-----------------------------------|------------------------|------------------------|--|--|
| Flu A/Cal/7/09 H1N1 [Day 28] | 646.8 (534.6 to 782.6) | 0 (0 to 0) | | |
| Flu B/Bri/60/08 Victoria [Day 0] | 22.2 (14.7 to 33.5) | 21 (14.8 to 30) | | |
| Flu B/Bri/60/08 Victoria [Day 28] | 320.1 (216.8 to 472.6) | 0 (0 to 0) | | |
| Flu A/Vic/210/09 H3N2 [Day 0] | 20 (13 to 30.8) | 279.2 (202.1 to 385.8) | | |
| Flu A/Vic/210/09 H3N2 [Day 28] | 20.3 (13.9 to 29.8) | 0 (0 to 0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean antibody titres for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains.

| | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------|
| End point title | Geometric mean antibody titres for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains. |
| End point description: | |
| Fluarix vaccine strains were Flu A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2) and B/Brisbane/60/2008. Only data for the Flu A/California/7/2009 (H1N1) strain were presented for the Havrix Group. Titres were expressed as geometric mean antibody titres (GMTs). | |
| End point type | Secondary |
| End point timeframe: | |
| At Day 0 and at Month 6 | |

| End point values | Fluarix Group | Havrix Group | | |
|------------------------------------------|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 35 | 37 | | |
| Units: Titres | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Flu B/Bri/60/08 Victoria [Day 0] | 22.9 (15.6 to 33.8) | 0 (0 to 0) | | |
| Flu B/Bri/60/08 Victoria [Month 6] | 242.4 (173.9 to 337.8) | 0 (0 to 0) | | |
| Flu A/Cal/7/09 H1N1 [Day 0] | 169.7 (116.2 to 247.8) | 152.7 (105.6 to 220.8) | | |
| Flu A/Cal/7/09 H1N1 [Month 6] | 346.4 (273.4 to 438.8) | 131.4 (92.5 to 186.6) | | |
| Flu A/Vic/210/09 H3N2 [Day 0] | 17.9 (12.7 to 25.3) | 0 (0 to 0) | | |
| Flu A/Vic/210/09 H3N2 [Month 6] | 160.1 (118.1 to 217) | 0 (0 to 0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains.

| | |
|-----------------|-----------------------------------------------------------------------------------------------------------------------|
| End point title | Number of seropositive subjects for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains. |
|-----------------|-----------------------------------------------------------------------------------------------------------------------|

End point description:

Fluarix vaccine strains were Flu A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2) and B/Brisbane/60/2008. Seropositivity was assessed for subjects with an antibody titre assay cut-off value equal to or above 1:10. Day 28 data were presented for the Fluarix Group only.

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

End point timeframe:

At Day 0 and Day 28

| End point values | Fluarix Group | Havrix Group | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 33 | 39 | | |
| Units: Subjects | | | | |
| Flu A/Cal/7/09 H1N1 [Day 0] | 33 | 39 | | |
| Flu A/Cal/7/09 H1N1 [Day 28] | 33 | 0 | | |
| Flu B/Bri/60/08 Victoria [Day 0] | 26 | 31 | | |
| Flu B/Bri/60/08 Victoria [Day 28] | 33 | 0 | | |
| Flu A/Vic/210/09 H3N2 [Day 0] | 24 | 28 | | |
| Flu A/Vic/210/09 H3N2 [Day 28] | 33 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains.

| | |
|-----------------|-----------------------------------------------------------------------------------------------------------------------|
| End point title | Number of seropositive subjects for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains. |
|-----------------|-----------------------------------------------------------------------------------------------------------------------|

End point description:

Fluarix vaccine strains were Flu A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2) and B/Brisbane/60/2008. Seropositivity was assessed for subjects with an antibody titre assay cut-off equal to or above 1:10. Only data for the Flu A/California/7/2009 (H1N1) strain were presented for the Havrix Group.

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

End point timeframe:

At Day 0 and at Month 6

| End point values | Fluarix Group | Havrix Group | | |
|------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 35 | 37 | | |
| Units: Subjects | | | | |
| Flu B/Bri/60/08 Victoria [Day 0] | 29 | 0 | | |
| Flu B/Bri/60/08 Victoria [Month 6] | 35 | 0 | | |
| Flu A/Cal/7/09 H1N1 [Day 0] | 35 | 37 | | |
| Flu A/Cal/7/09 H1N1 [Month 6] | 35 | 37 | | |
| Flu A/Vic/210/09 H3N2 [Day 0] | 25 | 0 | | |
| Flu A/Vic/210/09 H3N2 [Month 6] | 35 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains.

| | |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of seroconverted subjects for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains. ^[8] |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Fluarix vaccine strains were Flu A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2) and B/Brisbane/60/2008. A seroconverted subject was a subject who had either a pre-vaccination (Day 0) titre less than ($<$) 1:10 and a post-vaccination titre greater than or equal to (\geq) 1:40 or a pre-vaccination titre \geq 1:10 and at least a 4-fold increase in post-vaccination titre. Day 28 data were presented for the Fluarix Group only.

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

End point timeframe:

At Day 28

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Day 28 data were presented for the Fluarix Group only.

| End point values | Fluarix Group | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 33 | | | |
| Units: Subjects | | | | |
| Flu A/Cal/7/09 H1N1 | 16 | | | |
| Flu B/Bri/60/08 Victoria | 28 | | | |
| Flu A/Vic/210/09 H3N2 | 29 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains.

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

End point description:

Fluarix vaccine strains were Flu A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2) and B/Brisbane/60/2008. A seroconverted subject was a subject who had either a pre-vaccination (Day 0) titre < 1:10 and a post-vaccination titre ≥ 1:40 or a pre-vaccination titre ≥ 1:10 and at least a 4-fold increase in post-vaccination titre. Only data for the Flu A/California/7/2009 (H1N1) strain were presented for the Havrix Group.

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

End point timeframe:

At Month 6

| End point values | Fluarix Group | Havrix Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 35 | 37 | | |
| Units: Subjects | | | | |
| Flu B/Bri/60/08 Victoria | 29 | 0 | | |
| Flu A/Cal/7/09 H1N1 | 8 | 2 | | |
| Flu A/Vic/210/09 H3N2 | 30 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains.

| | |
|-----------------|------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of seroprotected subjects for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains. |
|-----------------|------------------------------------------------------------------------------------------------------------------------|

End point description:

Fluarix vaccine strains were Flu A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2) and B/Brisbane/60/2008. A seroprotected subject was a subject with a serum HI titre ≥ 1:40 that usually is accepted as indicating protection. Day 28 data were presented for the Fluarix Group only.

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

End point timeframe:

At Day 0 and Day 28

| End point values | Fluarix Group | Havrix Group | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 33 | 39 | | |
| Units: Subjects | | | | |
| Flu A/Cal/7/09 H1N1 [Day 0] | 31 | 36 | | |
| Flu A/Cal/7/09 H1N1 [Day 28] | 33 | 0 | | |
| Flu B/Bri/60/08 Victoria [Day 0] | 13 | 11 | | |
| Flu B/Bri/60/08 Victoria [Day 28] | 33 | 0 | | |
| Flu A/Vic/210/09 H3N2 [Day 0] | 12 | 16 | | |
| Flu A/Vic/210/09 H3N2 [Day 28] | 33 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains.

| | |
|-----------------|------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of seroprotected subjects for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains. |
|-----------------|------------------------------------------------------------------------------------------------------------------------|

End point description:

Fluarix vaccine strains were Flu A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2) and B/Brisbane/60/2008. A seroprotected subject was a subject with a serum HI titre $\geq 1:40$ that usually is accepted as indicating protection. Only data for the Flu A/California/7/2009 (H1N1) strain were presented for the Havrix Group.

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

End point timeframe:

At Day 0 and Month 6

| End point values | Fluarix Group | Havrix Group | | |
|------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 35 | 37 | | |
| Units: Subjects | | | | |
| Flu B/Bri/60/08 Victoria [Day 0] | 13 | 0 | | |
| Flu B/Bri/60/08 Victoria [Month 6] | 33 | 0 | | |
| Flu A/Cal/7/09 H1N1 [Day 0] | 33 | 34 | | |
| Flu A/Cal/7/09 H1N1 [Month 6] | 35 | 34 | | |
| Flu A/Vic/210/09 H3N2 [Day 0] | 13 | 0 | | |
| Flu A/Vic/210/09 H3N2 [Month 6] | 34 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean geometric increase (MGI) for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains.

| | |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Mean geometric increase (MGI) for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains. ^[9] |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Fluarix vaccine strains were Flu A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2) and B/Brisbane/60/2008. MGI is defined as the geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the pre-vaccination (Day 0) reciprocal HI titre. Day 28 data were presented for the Fluarix Group only.

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

End point timeframe:

At Day 28

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Day 28 data were presented for the Fluarix Group only.

| End point values | Fluarix Group | | | |
|------------------------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 33 | | | |
| Units: Ratio | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Flu A/Cal/7/09 H1N1 | 4.3 (2.9 to 6.4) | | | |
| Flu B/Bri/60/08 Victoria | 14.4 (9.4 to 22) | | | |
| Flu A/Vic/210/09 H3N2 | 14 (9.3 to 21.1) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean geometric increase (MGI) for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains.

| | |
|-----------------|---------------------------------------------------------------------------------------------------------------------|
| End point title | Mean geometric increase (MGI) for haemagglutination inhibition (HI) antibodies against all Fluarix vaccine strains. |
|-----------------|---------------------------------------------------------------------------------------------------------------------|

End point description:

Fluarix vaccine strains were Flu A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2) and B/Brisbane/60/2008. MGI is defined as the geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the pre-vaccination (Day 0) reciprocal HI titre. Only data for the Flu A/California/7/2009 (H1N1) strain were presented for the Havrix Group.

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

End point timeframe:

At Month 6

| End point values | Fluarix Group | Havrix Group | | |
|------------------------------------------|--------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 35 | 37 | | |
| Units: Ratio | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Flu B/Bri/60/08 Victoria | 10.6 (7.5 to 14.9) | 0 (0 to 0) | | |
| Flu A/Cal/7/09 H1N1 | 2 (1.6 to 2.7) | 0.9 (0.7 to 1.1) | | |
| Flu A/Vic/210/09 H3N2 | 8.9 (6.6 to 12) | 0 (0 to 0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean antibody titres for neutralising antibodies against all Fluarix vaccine strains.

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
| End point title | Geometric mean antibody titres for neutralising antibodies against all Fluarix vaccine strains. |
| End point description: Fluarix vaccine strains were Flu A/California/7/2009 (H1N1), A/Perth/16/09(H3N2) and B/Brisbane/60/2008. Day 28 data were presented for the Fluarix Group only. Titres were expressed as geometric mean antibody titres (GMTs). | |
| End point type | Secondary |
| End point timeframe: At Day 0 and at Day 28 | |

| End point values | Fluarix Group | Havrix Group | | |
|------------------------------------------|---------------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 33 | 39 | | |
| Units: Titre | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Flu B/Bri/60/08 Victoria [Day 0] | 26 (20.2 to 33.6) | 24.5 (18.9 to 31.9) | | |
| Flu B/Bri/60/08 Victoria [Day 28] | 257.9 (158.5 to 419.5) | 0 (0 to 0) | | |
| Flu A/Cal/7/09 H1N1 [Day 0] | 119.7 (95.2 to 150.5) | 137.7 (108 to 175.5) | | |
| Flu A/Cal/7/09 H1N1 [Day 28] | 1512.4 (1077.9 to 2122.1) | 0 (0 to 0) | | |
| Flu A/Per/16/09 H3N2 [Day 0] | 69.8 (50.5 to 96.5) | 72.6 (55.2 to 95.5) | | |
| Flu A/Per/16/09 H3N2 [Day 28] | 614.5 (371.4 to 1016.7) | 0 (0 to 0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean antibody titres for neutralising antibodies against all Fluarix vaccine strains.

| | |
|-----------------|-------------------------------------------------------------------------------------------------|
| End point title | Geometric mean antibody titres for neutralising antibodies against all Fluarix vaccine strains. |
|-----------------|-------------------------------------------------------------------------------------------------|

End point description:

Fluarix vaccine strains were Flu A/California/7/2009 (H1N1), A/Perth/16/09 (H3N2) and B/Brisbane/60/2008. Titres were expressed as geometric mean antibody titres (GMTs). Only data for the Flu A/California/7/2009 (H1N1) strain were presented for the Havrix Group.

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

End point timeframe:

At Day 0 and at Month 6

| End point values | Fluarix Group | Havrix Group | | |
|------------------------------------------|------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 35 | 37 | | |
| Units: Titre | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Flu B/Bri/60/08 Victoria [Day 0] | 25.1 (19.7 to 32.1) | 0 (0 to 0) | | |
| Flu B/Bri/60/08 Victoria [Month 6] | 199.5 (145.8 to 273) | 0 (0 to 0) | | |
| Flu A/Cal/7/09 H1N1 [Day 0] | 119.4 (94.5 to 150.8) | 138.3 (107.5 to 178) | | |
| Flu A/Cal/7/09 H1N1 [Month 6] | 390.6 (291.4 to 523.8) | 115.3 (82.4 to 161.4) | | |
| Flu A/Per/16/09 H3N2 [Day 0] | 62.5 (49.5 to 78.8) | 0 (0 to 0) | | |
| Flu A/Per/16/09 H3N2 [Month 6] | 266.8 (173.6 to 410.1) | 0 (0 to 0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for neutralising antibodies against all Fluarix vaccine strains.

| | |
|-----------------|-------------------------------------------------------------------------------------------------------------------|
| End point title | Number of seroconverted subjects for neutralising antibodies against all Fluarix vaccine strains. ^[10] |
|-----------------|-------------------------------------------------------------------------------------------------------------------|

End point description:

A seroconverted subject for neutralising antibodies was a subject with a minimum 4-fold increase in titre at post-vaccination. Fluarix vaccine strains were Flu A/California/7/2009 (H1N1), A/Perth/16/09 (H3N2) and B/Brisbane/60/2008. Day 28 data were presented for the Fluarix Group only.

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

End point timeframe:

At Day 28

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Day 28 data were presented for the Fluarix Group only.

| End point values | Fluarix Group | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 33 | | | |
| Units: Subjects | | | | |
| Flu B/Bri/60/08 Victoria | 25 | | | |
| Flu A/Cal/7/09 H1N1 | 29 | | | |
| Flu A/Per/16/09 H3N2 | 22 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for neutralising antibodies against all Fluarix vaccine strains.

| | |
|-----------------|---------------------------------------------------------------------------------------------------|
| End point title | Number of seroconverted subjects for neutralising antibodies against all Fluarix vaccine strains. |
|-----------------|---------------------------------------------------------------------------------------------------|

End point description:

A seroconverted subject for neutralising antibodies was a subject with a minimum 4-fold increase in titre at post-vaccination. Fluarix vaccine strains were Flu A/California/7/2009 (H1N1), A/Perth/16/09 (H3N2) and B/Brisbane/60/2008. At Month 6, only data for the Flu A/California/7/2009 (H1N1) strain were presented for the Havrix Group.

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

End point timeframe:

At Month 6

| End point values | Fluarix Group | Havrix Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 35 | 37 | | |
| Units: Subjects | | | | |
| Flu B/Bri/60/08 Victoria | 28 | 0 | | |
| Flu A/Cal/7/09 H1N1 | 13 | 2 | | |
| Flu A/Per/16/09 H3N2 | 17 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and Grade 3 solicited local symptoms.

| | |
|-----------------|------------------------------------------------------------------------|
| End point title | Number of subjects reporting any and Grade 3 solicited local symptoms. |
|-----------------|------------------------------------------------------------------------|

End point description:

Solicited local symptoms assessed were pain, redness and swelling. Any = occurrence of any solicited local symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling above 50 millimetres.

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

End point timeframe:

Within 7 days (Day 0 – Day 6) after vaccination

| End point values | Fluarix Group | Havrix Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 38 | 39 | | |
| Units: Subjects | | | | |
| Any pain | 35 | 24 | | |
| Grade 3 pain | 2 | 0 | | |
| Any redness | 6 | 5 | | |
| Grade 3 redness | 0 | 0 | | |
| Any swelling | 5 | 0 | | |
| Grade 3 swelling | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and Grade 3 solicited general symptoms.

| | |
|-----------------|--------------------------------------------------------------------------|
| End point title | Number of subjects reporting any and Grade 3 solicited general symptoms. |
|-----------------|--------------------------------------------------------------------------|

End point description:

Solicited general symptoms assessed were arthralgia, fatigue, gastrointestinal symptoms, headache, myalgia, shivering, sweating, temperature (temperature = axillary temperature equal to or above 37.5 degrees Celsius). Any = occurrence of any solicited general symptom regardless of intensity grade or relation to vaccination. Grade 3 symptom = general symptom that prevented normal activity. Grade 3 temperature = axillary temperature above 39.0 degrees Celsius.

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

End point timeframe:

Within 7 days (Day 0 – Day 6) after vaccination

| End point values | Fluarix Group | Havrix Group | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 38 | 39 | | |
| Units: Subjects | | | | |
| Any arthralgia | 4 | 5 | | |
| Grade 3 arthralgia | 0 | 0 | | |
| Any fatigue | 25 | 24 | | |
| Grade 3 fatigue | 1 | 1 | | |
| Any gastrointestinal symptoms | 8 | 3 | | |
| Grade 3 gastrointestinal symptoms | 2 | 0 | | |
| Any headache | 24 | 16 | | |
| Grade 3 headache | 1 | 0 | | |

| | | | | |
|----------------------------------------------|----|----|--|--|
| Any myalgia | 16 | 16 | | |
| Grade 3 myalgia | 0 | 1 | | |
| Any shivering | 18 | 9 | | |
| Grade 3 shivering | 0 | 0 | | |
| Any sweating | 9 | 4 | | |
| Grade 3 sweating | 0 | 0 | | |
| Any temperature $\geq 37.5^{\circ}\text{C}$ | 4 | 1 | | |
| Grade 3 temperature $> 39.0^{\circ}\text{C}$ | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of days with any solicited local symptoms.

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| End point title | Number of days with any solicited local symptoms. |
| End point description: Solicited local symptoms assessed were pain, redness and swelling. Inter-quartile range assessed was the 25th percentile and the 75th percentile. | |
| End point type | Secondary |
| End point timeframe: Within 7 days (Day 0 – Day 6) after vaccination | |

| End point values | Fluarix Group | Havrix Group | | |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 38 | 39 | | |
| Units: Days | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| Pain | 2 (1 to 3) | 2 (1 to 2.5) | | |
| Redness | 2 (1 to 2) | 1 (1 to 2) | | |
| Swelling | 2 (2 to 3) | 0 (0 to 0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of days with grade 3 solicited local symptoms.

| | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|
| End point title | Number of days with grade 3 solicited local symptoms. |
| End point description: Solicited local symptoms assessed were pain and swelling. Grade 3 redness/swelling = redness/swelling above 50 millimetres. Inter-quartile range assessed was the 25th percentile and the 75th percentile. | |
| End point type | Secondary |
| End point timeframe: Within 7 days (Day 0 – Day 6) after vaccination | |

| End point values | Fluarix Group | Havrix Group | | |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 38 | 39 | | |
| Units: Days | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| Pain | 1 (1 to 1) | 0 (0 to 0) | | |
| Swelling | 1 (1 to 1) | 0 (0 to 0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of days with any solicited general symptoms.

| | |
|-----------------|-----------------------------------------------------|
| End point title | Number of days with any solicited general symptoms. |
|-----------------|-----------------------------------------------------|

End point description:

Solicited general symptoms assessed were arthralgia, fatigue, gastrointestinal symptoms, headache, myalgia, shivering, sweating, temperature (temperature = axillary temperature equal to or above 37.5 degrees Celsius). Inter-quartile range assessed was the 25th percentile and the 75th percentile.

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

End point timeframe:

Within 7 days (Day 0 – Day 6) after vaccination

| End point values | Fluarix Group | Havrix Group | | |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 38 | 39 | | |
| Units: Days | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| Arthralgia | 2 (1.5 to 4) | 1 (1 to 2) | | |
| Fatigue | 2 (1 to 4) | 2 (1 to 3) | | |
| Gastrointestinal | 1 (1 to 2) | 1 (1 to 3) | | |
| Headache | 2 (1 to 3) | 1 (1 to 2) | | |
| Myalgia | 2 (1.5 to 3.5) | 2 (1 to 3) | | |
| Sweating | 1 (1 to 1) | 2 (2 to 2.5) | | |
| Shivering | 2 (1 to 4) | 1 (1 to 1) | | |
| Temperature | 1 (1 to 1.5) | 1 (1 to 1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of days with grade 3 solicited general symptoms.

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------|
| End point title | Number of days with grade 3 solicited general symptoms. |
| End point description: | |
| Solicited general symptoms assessed were fatigue, gastrointestinal symptoms, headache and myalgia. Grade 3 symptom = general symptom that prevented normal activity. Inter-quartile range assessed was the 25th percentile and the 75th percentile. | |
| End point type | Secondary |
| End point timeframe: | |
| Within 7 days (Day 0 – Day 6) after vaccination | |

| End point values | Fluarix Group | Havrix Group | | |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 38 | 39 | | |
| Units: Days | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| Fatigue | 1 (1 to 1) | 1 (1 to 1) | | |
| Gastrointestinal | 1 (1 to 1) | 0 (0 to 0) | | |
| Headache | 1 (1 to 1) | 0 (0 to 0) | | |
| Myalgia | 0 (0 to 0) | 1 (1 to 1) | | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| End point title | Number of subjects reporting any, grade 3 and related unsolicited adverse events (AEs). |
| End point description: | |
| An unsolicited adverse event is any adverse event (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. Grade 3 = event that prevented normal, everyday activities. Related = event assessed by the investigator as causally related to the study vaccination. | |
| End point type | Secondary |
| End point timeframe: | |
| Within 28 days (Day 0 – Day 27) after vaccination | |

| End point values | Fluarix Group | Havrix Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 38 | 39 | | |
| Units: Subjects | | | | |
| Any | 12 | 11 | | |
| Grade 3 | 1 | 2 | | |

| | | | | |
|------------------------|---|---|--|--|
| Related to vaccination | 4 | 1 | | |
|------------------------|---|---|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting medically-attended events (MAEs).

| | |
|-----------------|----------------------------------------------------------------|
| End point title | Number of subjects reporting medically-attended events (MAEs). |
|-----------------|----------------------------------------------------------------|

End point description:

For each solicited and unsolicited symptom the subject experienced, the subject was asked if they received medical attention defined as hospitalization, an emergency room visit or a visit to or from medical personnel for any reason.

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

End point timeframe:

Within the 28-day (Days 0-27) post-vaccination period

| End point values | Fluarix Group | Havrix Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 38 | 39 | | |
| Units: Subjects | | | | |
| MAEs Number | 1 | 3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting medically-attended events (MAEs).

| | |
|-----------------|----------------------------------------------------------------|
| End point title | Number of subjects reporting medically-attended events (MAEs). |
|-----------------|----------------------------------------------------------------|

End point description:

For each solicited and unsolicited symptom the subject experienced, the subject was asked if they received medical attention defined as hospitalization, an emergency room visit or a visit to or from medical personnel for any reason.

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

End point timeframe:

During the entire study period (Up to Month 6)

| End point values | Fluarix Group | Havrix Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 38 | 39 | | |
| Units: Subjects | | | | |
| MAE(s) Number | 2 | 4 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting adverse events of specific interest (AESIs)/potential immune mediated diseases (pIMDs).

| | |
|-----------------|----------------------------------------------------------------------------------------------------------------------|
| End point title | Number of subjects reporting adverse events of specific interest (AESIs)/potential immune mediated diseases (pIMDs). |
|-----------------|----------------------------------------------------------------------------------------------------------------------|

End point description:

Potential Immune-Mediated Diseases (pIMDs) or Adverse events of specific interest (AESI), are a subset of AEs that include both clearly autoimmune diseases and also other inflammatory and/or neurologic disorders which may or may not have an autoimmune etiology.

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

End point timeframe:

During the entire study period (Up to Month 6)

| End point values | Fluarix Group | Havrix Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 38 | 39 | | |
| Units: Subjects | | | | |
| AESIs/pIMDs Number | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting adverse events of special interest.

| | |
|-----------------|------------------------------------------------------------------|
| End point title | Number of subjects reporting adverse events of special interest. |
|-----------------|------------------------------------------------------------------|

End point description:

Adverse events of special interest for safety monitoring includes both convulsion and anaphylaxis.

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

End point timeframe:

During the entire study period (Up to Month 6)

| End point values | Fluarix Group | Havrix Group | | |
|--------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 38 | 39 | | |
| Units: Subjects | | | | |
| AEs of special interest Number | 0 | 0 | | |

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:

SAEs assessed include medical occurrences that results in death, are life threatening, require hospitalization or prolongation of hospitalization, results in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subjects.

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

End point timeframe:

Within the 28-day (Days 0-27) post-vaccination period

| End point values | Fluarix Group | Havrix Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 38 | 39 | | |
| Units: Subjects | | | | |
| Any SAE(s) | 0 | 0 | | |

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:

SAEs assessed include medical occurrences that results in death, are life threatening, require hospitalization or prolongation of hospitalization, results in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subjects.

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

End point timeframe:

During the entire study period (Up to Month 6)

| | | | | |
|-----------------------------|-----------------|-----------------|--|--|
| End point values | Fluarix Group | Havrix Group | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 38 | 39 | | |
| Units: Subjects | | | | |
| Any SAE(s) | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events were assessed up to Day 28 and during the entire study period, up to Month 6. Systematically and non-systematically assessed frequent adverse events were assessed during the 7 day and 28 day post-vaccination period respectively.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 14.0 |
|--------------------|------|

Reporting groups

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| Reporting group title | Havrix Group |
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Reporting group description:

Subjects previously vaccinated with Pandemrix vaccine received 1 first dose of Havrix vaccine (subjects aged above 15 years) or Havrix-Junior vaccine (subjects aged 15 years and below). A second dose was given outside the study setting, at Month 6. All vaccines were administered in the deltoid region of the non-dominant arm on Day 0.

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|-----------------------|---------------|
| Reporting group title | Fluarix Group |
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Reporting group description:

Subjects previously vaccinated with Pandemrix vaccine received 1 dose of Fluarix vaccine. All vaccines were administered in the deltoid region of the non-dominant arm on Day 0.

| Serious adverse events | Havrix Group | Fluarix Group | |
|---------------------------------------------------|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 38 (2.63%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Infections and infestations | | | |
| Acute tonsillitis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 38 (2.63%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Havrix Group | Fluarix Group | |
|-------------------------------------------------------|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 24 / 39 (61.54%) | 35 / 38 (92.11%) | |
| Nervous system disorders | | | |
| Headache (AE) | | | |

| | | | |
|------------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed | 2 / 39 (5.13%) | 1 / 38 (2.63%) | |
| occurrences (all) | 2 | 1 | |
| General disorders and administration site conditions | | | |
| Pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 24 / 39 (61.54%) | 35 / 38 (92.11%) | |
| occurrences (all) | 24 | 35 | |
| Redness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | 6 / 38 (15.79%) | |
| occurrences (all) | 5 | 6 | |
| Swelling | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 5 / 38 (13.16%) | |
| occurrences (all) | 0 | 5 | |
| Arthralgia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | 4 / 38 (10.53%) | |
| occurrences (all) | 5 | 4 | |
| Fatigue | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 24 / 39 (61.54%) | 25 / 38 (65.79%) | |
| occurrences (all) | 24 | 25 | |
| Gastrointestinal symptoms | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 8 / 38 (21.05%) | |
| occurrences (all) | 3 | 8 | |
| Headache (Solicited Symptom) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 16 / 39 (41.03%) | 24 / 38 (63.16%) | |
| occurrences (all) | 16 | 24 | |
| Myalgia | | | |
| alternative assessment type: Systematic | | | |

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| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Shivering</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Sweating</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Temperature</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>16 / 39 (41.03%)</p> <p>16</p> <p>9 / 39 (23.08%)</p> <p>9</p> <p>4 / 39 (10.26%)</p> <p>4</p> <p>1 / 39 (2.56%)</p> <p>1</p> | <p>16 / 38 (42.11%)</p> <p>16</p> <p>18 / 38 (47.37%)</p> <p>18</p> <p>9 / 38 (23.68%)</p> <p>9</p> <p>4 / 38 (10.53%)</p> <p>4</p> | |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Oropharyngeal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 39 (5.13%)</p> <p>2</p> | <p>1 / 38 (2.63%)</p> <p>1</p> | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Neck pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 39 (0.00%)</p> <p>0</p> | <p>2 / 38 (5.26%)</p> <p>2</p> | |
| <p>Infections and infestations</p> <p>Upper respiratory tract infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 39 (5.13%)</p> <p>2</p> | <p>3 / 38 (7.89%)</p> <p>3</p> | |

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