



## Clinical trial results:

**A phase II, observer-blinded, multi-center, controlled study to assess the safety and immunogenicity of one dose of GlaxoSmithKline (GSK) Biologicals' meningococcal serogroup ACWY tetanus toxoid conjugate vaccine (MenACWY-TT) versus one dose of sanofi pasteur's meningococcal serogroups A, C, W-135 and Y vaccine (Menactra®) in healthy subjects aged 10 through 25 years.**

## Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2012-001305-25 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 29 July 2011   |

## Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1           |
| This version publication date  | 11 May 2016  |
| First version publication date | 29 July 2015 |

## Trial information

### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 114249 |
|-----------------------|--------|

### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01165242 |
| 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                       | 12 January 2012  |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 25 February 2011 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 29 July 2011     |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

- To demonstrate the non-inferiority of MenACWY-TT (Lot A) vaccine when compared to MenACWY-DT vaccine in terms of the percentage of subjects with serum bactericidal assay using human complement against *Neisseria meningitidis* serogroup A (hSBA-MenA), serogroup C (hSBA-MenC), serogroup W-135 (hSBA-MenW-135) and serogroup Y (hSBA-MenY) vaccine response one month after vaccination.

Protection of trial subjects:

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.

Background therapy: -

Evidence for comparator: -

|                                                           |                |
|-----------------------------------------------------------|----------------|
| Actual start date of recruitment                          | 19 August 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 | United States: 713 |
| Country: Number of subjects enrolled | Canada: 300        |
| Worldwide total number of subjects   | 1013               |
| EEA total number of subjects         | 0                  |

Notes:

### Subjects enrolled per age group

|                                           |      |
|-------------------------------------------|------|
| In utero                                  | 0    |
| Preterm newborn - gestational age < 37 wk | 0    |
| Newborns (0-27 days)                      | 0    |
| Infants and toddlers (28 days-23 months)  | 0    |
| Children (2-11 years)                     | 0    |
| Adolescents (12-17 years)                 | 1013 |
| 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.

### Pre-assignment period milestones

|                              |      |
|------------------------------|------|
| Number of subjects started   | 1013 |
| Number of subjects completed | 1011 |

### Pre-assignment subject non-completion reasons

|                            |                            |
|----------------------------|----------------------------|
| Reason: Number of subjects | No vaccination received: 2 |
|----------------------------|----------------------------|

### Period 1

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

Blinding implementation details:

Data were collected in an observer-blind manner during this study. The blinding was observer-blind with respect to lots of MenACWY-TT and observer-blind with respect to MenACWY-TT or Menactra. By observer-blind, it was meant that during the course of the study, the vaccine recipient and those responsible for the evaluation of any study endpoint (e.g. safety and reactogenicity) were all unaware of which vaccine was administered.

### Arms

|                              |                   |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes               |
| <b>Arm title</b>             | Nimenrix™ A Group |

Arm description:

Subjects received 1 dose of Nimenrix™ Lot A vaccine.

|                                        |                                  |
|----------------------------------------|----------------------------------|
| Arm type                               | Experimental                     |
| Investigational medicinal product name | Nimenrix™                        |
| Investigational medicinal product code |                                  |
| Other name                             | Meningococcal vaccine GSK 134612 |
| Pharmaceutical forms                   | Injection                        |
| Routes of administration               | Intramuscular use                |

Dosage and administration details:

One intramuscular injection administered in the deltoid region of the non-dominant arm.

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | Nimenrix™ B Group |
|------------------|-------------------|

Arm description:

Subjects received 1 dose of Nimenrix™ Lot B vaccine.

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

|                                                                                         |                                  |
|-----------------------------------------------------------------------------------------|----------------------------------|
| Investigational medicinal product name                                                  | Nimenrix™                        |
| Investigational medicinal product code                                                  |                                  |
| Other name                                                                              | Meningococcal vaccine GSK 134612 |
| Pharmaceutical forms                                                                    | Injection                        |
| Routes of administration                                                                | Intramuscular use                |
| Dosage and administration details:                                                      |                                  |
| One intramuscular injection administered in the deltoid region of the non-dominant arm. |                                  |
| <b>Arm title</b>                                                                        | Menactra®MenACWY-DT Group        |

Arm description:

Subjects were vaccinated with Menactra®

|                                        |                    |
|----------------------------------------|--------------------|
| Arm type                               | Active comparator  |
| Investigational medicinal product name | Menactra®          |
| Investigational medicinal product code |                    |
| Other name                             | MenACWY-DT vaccine |
| Pharmaceutical forms                   | Injection          |
| Routes of administration               | Intramuscular use  |

Dosage and administration details:

One intramuscular injection administered in the deltoid region of the non-dominant arm.

| <b>Number of subjects in period 1</b> <sup>[1]</sup> | Nimenrix™ A Group | Nimenrix™ B Group | Menactra®MenACWY-DT Group |
|------------------------------------------------------|-------------------|-------------------|---------------------------|
| Started                                              | 337               | 336               | 338                       |
| Completed                                            | 327               | 326               | 324                       |
| Not completed                                        | 10                | 10                | 14                        |
| Consent withdrawn by subject                         | -                 | 2                 | 2                         |
| 'Subjects unreachable '                              | 1                 | -                 | -                         |
| 'Subject incarcerated '                              | -                 | 1                 | -                         |
| Extended holiday                                     | -                 | -                 | 1                         |
| Lost to follow-up                                    | 9                 | 7                 | 10                        |
| Subject refuses visit 2                              | -                 | -                 | 1                         |

Notes:

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

Justification: Out of the 1013 subjects enrolled in this study, 2 were assigned subject numbers but received no vaccination and were hence excluded from the study start.

## Baseline characteristics

### Reporting groups

|                                                      |                           |
|------------------------------------------------------|---------------------------|
| Reporting group title                                | Nimenrix™ A Group         |
| Reporting group description:                         |                           |
| Subjects received 1 dose of Nimenrix™ Lot A vaccine. |                           |
| Reporting group title                                | Nimenrix™ B Group         |
| Reporting group description:                         |                           |
| Subjects received 1 dose of Nimenrix™ Lot B vaccine. |                           |
| Reporting group title                                | Menactra®MenACWY-DT Group |
| Reporting group description:                         |                           |
| Subjects were vaccinated with Menactra®              |                           |

| Reporting group values                                                                                                                                                                                                                                    | Nimenrix™ A Group | Nimenrix™ B Group | Menactra®MenACWY-DT Group |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|-------------------|---------------------------|
| Number of subjects                                                                                                                                                                                                                                        | 337               | 336               | 338                       |
| Age categorical<br>Units: Subjects                                                                                                                                                                                                                        |                   |                   |                           |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over |                   |                   |                           |
| Age continuous<br>Units: years                                                                                                                                                                                                                            |                   |                   |                           |
| arithmetic mean                                                                                                                                                                                                                                           | 16.4              | 16.3              | 16.2                      |
| standard deviation                                                                                                                                                                                                                                        | ± 5.16            | ± 5.16            | ± 4.97                    |
| Gender categorical<br>Units: Subjects                                                                                                                                                                                                                     |                   |                   |                           |
| Female                                                                                                                                                                                                                                                    | 175               | 169               | 176                       |
| Male                                                                                                                                                                                                                                                      | 162               | 167               | 162                       |

| Reporting group values                                                                                                                                                                                           | Total                           |  |  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|--|--|
| Number of subjects                                                                                                                                                                                               | 1011                            |  |  |
| Age categorical<br>Units: Subjects                                                                                                                                                                               |                                 |  |  |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years) | 0<br>0<br>0<br>0<br>0<br>0<br>0 |  |  |

|                   |   |  |  |
|-------------------|---|--|--|
| From 65-84 years  | 0 |  |  |
| 85 years and over | 0 |  |  |

|                                                                         |     |  |  |
|-------------------------------------------------------------------------|-----|--|--|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | -   |  |  |
| Gender categorical<br>Units: Subjects                                   |     |  |  |
| Female                                                                  | 520 |  |  |
| Male                                                                    | 491 |  |  |

## End points

### End points reporting groups

|                                                      |                           |
|------------------------------------------------------|---------------------------|
| Reporting group title                                | Nimenrix™ A Group         |
| Reporting group description:                         |                           |
| Subjects received 1 dose of Nimenrix™ Lot A vaccine. |                           |
| Reporting group title                                | Nimenrix™ B Group         |
| Reporting group description:                         |                           |
| Subjects received 1 dose of Nimenrix™ Lot B vaccine. |                           |
| Reporting group title                                | Menactra®MenACWY-DT Group |
| Reporting group description:                         |                           |
| Subjects were vaccinated with Menactra®              |                           |

### Primary: Number of subjects with vaccine response to hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibodies

|                                 |                                                                                                                             |
|---------------------------------|-----------------------------------------------------------------------------------------------------------------------------|
| End point title                 | Number of subjects with vaccine response to hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibodies <sup>[1][2]</sup> |
| End point description:          |                                                                                                                             |
| End point type                  | Primary                                                                                                                     |
| End point timeframe:            |                                                                                                                             |
| One month after the vaccination |                                                                                                                             |

#### Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

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

[2] - 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: Reporting for hSBA results was done separately for the baseline groups.

| End point values            | Nimenrix™ A Group | Menactra®Men ACWY-DT Group |  |  |
|-----------------------------|-------------------|----------------------------|--|--|
| Subject group type          | Reporting group   | Reporting group            |  |  |
| Number of subjects analysed | 310               | 297                        |  |  |
| Units: Subjects             |                   |                            |  |  |
| hSBA-MenA                   | 281               | 191                        |  |  |
| hSBA-MenC                   | 217               | 209                        |  |  |
| hSBA-MenW-135               | 198               | 185                        |  |  |
| hSBA-MenY                   | 150               | 115                        |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibody titers $\geq 1:4$

|                             |                                                                                                       |
|-----------------------------|-------------------------------------------------------------------------------------------------------|
| End point title             | Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibody titers $\geq$ 1:4 |
| End point description:      |                                                                                                       |
| End point type              | Secondary                                                                                             |
| End point timeframe:        |                                                                                                       |
| One month after vaccination |                                                                                                       |

| End point values            | Nimenrix™ A Group | Nimenrix™ B Group | Menactra®Men ACWY-DT Group |  |
|-----------------------------|-------------------|-------------------|----------------------------|--|
| Subject group type          | Reporting group   | Reporting group   | Reporting group            |  |
| Number of subjects analysed | 315               | 309               | 305                        |  |
| Units: Subjects             |                   |                   |                            |  |
| hSBA-MenA (POST)            | 253               | 243               | 223                        |  |
| hSBA-MenC (POST)            | 295               | 293               | 291                        |  |
| hSBA-MenW-135 (POST)        | 272               | 262               | 247                        |  |
| hSBA-MenY (POST)            | 307               | 302               | 287                        |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with vaccine response to hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibody titers $\geq$ 1:8

|                             |                                                                                                                           |
|-----------------------------|---------------------------------------------------------------------------------------------------------------------------|
| End point title             | Number of subjects with vaccine response to hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibody titers $\geq$ 1:8 |
| End point description:      |                                                                                                                           |
| End point type              | Secondary                                                                                                                 |
| End point timeframe:        |                                                                                                                           |
| One month after vaccination |                                                                                                                           |

| End point values            | Nimenrix™ A Group | Nimenrix™ B Group | Menactra®Men ACWY-DT Group |  |
|-----------------------------|-------------------|-------------------|----------------------------|--|
| Subject group type          | Reporting group   | Reporting group   | Reporting group            |  |
| Number of subjects analysed | 315               | 309               | 305                        |  |
| Units: Subjects             |                   |                   |                            |  |
| hSBA-MenA (POST)            | 251               | 242               | 221                        |  |
| hSBA-MenC (POST)            | 295               | 292               | 291                        |  |
| hSBA-MenW-135 (POST)        | 272               | 262               | 247                        |  |
| hSBA-MenY (POST)            | 307               | 302               | 287                        |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Concentration of hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibody titers

|                             |                                                                                     |
|-----------------------------|-------------------------------------------------------------------------------------|
| End point title             | Concentration of hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibody titers |
| End point description:      |                                                                                     |
| End point type              | Secondary                                                                           |
| End point timeframe:        |                                                                                     |
| One month after vaccination |                                                                                     |

| End point values                         | Nimenrix™ A Group      | Nimenrix™ B Group      | Menactra®Men ACWY-DT Group |  |
|------------------------------------------|------------------------|------------------------|----------------------------|--|
| Subject group type                       | Reporting group        | Reporting group        | Reporting group            |  |
| Number of subjects analysed              | 315                    | 309                    | 305                        |  |
| Units: Titers                            |                        |                        |                            |  |
| geometric mean (confidence interval 95%) |                        |                        |                            |  |
| hSBA-MenA (POST)                         | 54.2 (43.5 to 67.4)    | 49.6 (39.6 to 62.1)    | 41.3 (32.3 to 52.9)        |  |
| hSBA-MenC (POST)                         | 687.1 (510.5 to 924.9) | 755.8 (557.3 to 1025)  | 543.3 (411.2 to 718)       |  |
| hSBA-MenW-135 (POST)                     | 174.5 (138.6 to 219.6) | 161.6 (128.3 to 203.5) | 101.7 (77.9 to 132.7)      |  |
| hSBA-MenY (POST)                         | 349.1 (298.1 to 408.8) | 387.4 (329.7 to 455.1) | 253.8 (204.9 to 314.5)     |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with vaccine response for hSBA antibodies

|                             |                                                   |
|-----------------------------|---------------------------------------------------|
| End point title             | Number of subjects with vaccine response for hSBA |
| End point description:      |                                                   |
| End point type              | Secondary                                         |
| End point timeframe:        |                                                   |
| One month after vaccination |                                                   |

Notes:

[3] - 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: Reporting for hSBA results was done separately for the baseline groups.

| End point values            | Nimenrix™ B Group |  |  |  |
|-----------------------------|-------------------|--|--|--|
| Subject group type          | Reporting group   |  |  |  |
| Number of subjects analysed | 300               |  |  |  |
| Units: Subjects             |                   |  |  |  |
| hSBA-MenA MenACWY-TT-B      | 214               |  |  |  |
| hSBA-MenC MenACWY-TT-B      | 226               |  |  |  |
| hSBA-MenW- 135 MenACWY-TT-B | 196               |  |  |  |
| hSBA-MenY MenACWY-TT-B      | 150               |  |  |  |

### 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:

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

End point timeframe:

Within 4 days (Day 0 - Day 3) following vaccination.

| End point values            | Nimenrix™ A Group | Nimenrix™ B Group | Menactra®Men ACWY-DT Group |  |
|-----------------------------|-------------------|-------------------|----------------------------|--|
| Subject group type          | Reporting group   | Reporting group   | Reporting group            |  |
| Number of subjects analysed | 329               | 329               | 325                        |  |
| Units: Subjects             |                   |                   |                            |  |
| Pain                        | 169               | 167               | 180                        |  |
| Redness                     | 85                | 60                | 66                         |  |
| Swelling                    | 63                | 40                | 44                         |  |

### 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:

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

End point timeframe:

Within 4 days (Day 0 - Day 3) following vaccination.

| End point values            | Nimenrix™ A Group | Nimenrix™ B Group | Menactra®Men ACWY-DT Group |  |
|-----------------------------|-------------------|-------------------|----------------------------|--|
| Subject group type          | Reporting group   | Reporting group   | Reporting group            |  |
| Number of subjects analysed | 329               | 329               | 326                        |  |
| Units: Subjects             |                   |                   |                            |  |
| Fatigue                     | 96                | 94                | 89                         |  |
| Gastrointestinal            | 43                | 43                | 44                         |  |
| Headache                    | 86                | 87                | 83                         |  |
| Temperature (Orally)        | 17                | 14                | 16                         |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Occurrence of unsolicited non-serious adverse events

|                 |                                                      |
|-----------------|------------------------------------------------------|
| End point title | Occurrence of unsolicited non-serious adverse events |
|-----------------|------------------------------------------------------|

End point description:

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

End point timeframe:

Within 31 days (Day 0 to 30) following vaccination

| End point values            | Nimenrix™ A Group | Nimenrix™ B Group | Menactra®Men ACWY-DT Group |  |
|-----------------------------|-------------------|-------------------|----------------------------|--|
| Subject group type          | Reporting group   | Reporting group   | Reporting group            |  |
| Number of subjects analysed | 337               | 336               | 338                        |  |
| Units: Subjects             |                   |                   |                            |  |
| AE(s)                       | 105               | 76                | 85                         |  |

### Statistical analyses

No statistical analyses for this end point

**Secondary: Number of subjects with occurrence of new onset of chronic illness(es) (NOCI)**

|                 |                                                                               |
|-----------------|-------------------------------------------------------------------------------|
| End point title | Number of subjects with occurrence of new onset of chronic illness(es) (NOCI) |
|-----------------|-------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

From Month 0 through Month 6

| End point values            | Nimenrix™ A Group | Nimenrix™ B Group | Menactra®Men ACWY-DT Group |  |
|-----------------------------|-------------------|-------------------|----------------------------|--|
| Subject group type          | Reporting group   | Reporting group   | Reporting group            |  |
| Number of subjects analysed | 337               | 336               | 338                        |  |
| Units: Subjects             |                   |                   |                            |  |
| NOCIs                       | 3                 | 0                 | 0                          |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of subjects with serious adverse events (SAEs)**

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

End point description:

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

End point timeframe:

From Month 0 through Month 6

| End point values            | Nimenrix™ A Group | Nimenrix™ B Group | Menactra®Men ACWY-DT Group |  |
|-----------------------------|-------------------|-------------------|----------------------------|--|
| Subject group type          | Reporting group   | Reporting group   | Reporting group            |  |
| Number of subjects analysed | 337               | 336               | 338                        |  |
| Units: Subjects             |                   |                   |                            |  |
| All SAEs                    | 0                 | 0                 | 0                          |  |

**Statistical analyses**

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms during the 4-day post-vaccination period, Unsolicited AEs during the 31-day post-vaccination period, SAEs up to study end

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 10.0   |

### Reporting groups

|                                |                    |
|--------------------------------|--------------------|
| Reporting group title          | MenACWY-TT-A Group |
| Reporting group description: - |                    |
| Reporting group title          | MenACWY-TT-B Group |
| Reporting group description: - |                    |
| Reporting group title          | MenACWY-DT Group   |
| Reporting group description: - |                    |

| Serious adverse events                            | MenACWY-TT-A Group | MenACWY-TT-B Group | MenACWY-DT Group |
|---------------------------------------------------|--------------------|--------------------|------------------|
| Total subjects affected by serious adverse events |                    |                    |                  |
| subjects affected / exposed                       | 1 / 337 (0.30%)    | 5 / 336 (1.49%)    | 2 / 338 (0.59%)  |
| number of deaths (all causes)                     | 0                  | 0                  | 0                |
| number of deaths resulting from adverse events    |                    |                    |                  |
| Injury, poisoning and procedural complications    |                    |                    |                  |
| Jaw fracture                                      |                    |                    |                  |
| subjects affected / exposed                       | 0 / 337 (0.00%)    | 0 / 336 (0.00%)    | 1 / 338 (0.30%)  |
| occurrences causally related to treatment / all   | 0 / 0              | 0 / 0              | 0 / 1            |
| deaths causally related to treatment / all        | 0 / 0              | 0 / 0              | 0 / 0            |
| Post procedural haematoma                         |                    |                    |                  |
| subjects affected / exposed                       | 0 / 337 (0.00%)    | 0 / 336 (0.00%)    | 1 / 338 (0.30%)  |
| occurrences causally related to treatment / all   | 0 / 0              | 0 / 0              | 0 / 1            |
| deaths causally related to treatment / all        | 0 / 0              | 0 / 0              | 0 / 0            |
| Respiratory, thoracic and mediastinal disorders   |                    |                    |                  |
| Asthma                                            |                    |                    |                  |
| subjects affected / exposed                       | 1 / 337 (0.30%)    | 1 / 336 (0.30%)    | 0 / 338 (0.00%)  |
| occurrences causally related to treatment / all   | 0 / 1              | 0 / 1              | 0 / 0            |
| deaths causally related to treatment / all        | 0 / 0              | 0 / 0              | 0 / 0            |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| Hypoxia                                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 337 (0.00%) | 1 / 336 (0.30%) | 0 / 338 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                 |                 |                 |
| Appendicitis                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 337 (0.00%) | 2 / 336 (0.60%) | 0 / 338 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pneumonia                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 337 (0.00%) | 2 / 336 (0.60%) | 0 / 338 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Influenza                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 337 (0.00%) | 1 / 336 (0.30%) | 0 / 338 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Tooth infection                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 337 (0.00%) | 1 / 336 (0.30%) | 0 / 338 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

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

| <b>Non-serious adverse events</b>                     | MenACWY-TT-A Group | MenACWY-TT-B Group | MenACWY-DT Group   |
|-------------------------------------------------------|--------------------|--------------------|--------------------|
| Total subjects affected by non-serious adverse events |                    |                    |                    |
| subjects affected / exposed                           | 169 / 337 (50.15%) | 167 / 336 (49.70%) | 180 / 338 (53.25%) |
| General disorders and administration site conditions  |                    |                    |                    |
| Pain                                                  |                    |                    |                    |
| alternative assessment type: Systematic               |                    |                    |                    |
| subjects affected / exposed                           | 169 / 337 (50.15%) | 167 / 336 (49.70%) | 180 / 338 (53.25%) |
| occurrences (all)                                     | 169                | 167                | 180                |
| Redness                                               |                    |                    |                    |
| alternative assessment type: Systematic               |                    |                    |                    |

|                                            |                   |                   |                   |
|--------------------------------------------|-------------------|-------------------|-------------------|
| subjects affected / exposed                | 85 / 337 (25.22%) | 60 / 336 (17.86%) | 66 / 338 (19.53%) |
| occurrences (all)                          | 85                | 60                | 66                |
| Swelling                                   |                   |                   |                   |
| alternative assessment type:<br>Systematic |                   |                   |                   |
| subjects affected / exposed                | 63 / 337 (18.69%) | 40 / 336 (11.90%) | 44 / 338 (13.02%) |
| occurrences (all)                          | 63                | 40                | 44                |
| Fatigue                                    |                   |                   |                   |
| alternative assessment type:<br>Systematic |                   |                   |                   |
| subjects affected / exposed                | 96 / 337 (28.49%) | 94 / 336 (27.98%) | 89 / 338 (26.33%) |
| occurrences (all)                          | 96                | 94                | 89                |
| Gastrointestinal                           |                   |                   |                   |
| alternative assessment type:<br>Systematic |                   |                   |                   |
| subjects affected / exposed                | 43 / 337 (12.76%) | 43 / 336 (12.80%) | 44 / 338 (13.02%) |
| occurrences (all)                          | 43                | 43                | 44                |
| Headache                                   |                   |                   |                   |
| alternative assessment type:<br>Systematic |                   |                   |                   |
| subjects affected / exposed                | 86 / 337 (25.52%) | 87 / 336 (25.89%) | 83 / 338 (24.56%) |
| occurrences (all)                          | 86                | 87                | 83                |
| Temperature (Orally)                       |                   |                   |                   |
| alternative assessment type:<br>Systematic |                   |                   |                   |
| subjects affected / exposed                | 17 / 337 (5.04%)  | 14 / 336 (4.17%)  | 16 / 338 (4.73%)  |
| occurrences (all)                          | 17                | 14                | 16                |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|-------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 16 March 2010     | <p>Amendment 3</p> <p>The introduction was updated with the current licensing status of competitor vaccines and the current recommendations for meningococcal vaccines.</p> <p>The primary objective of the current study is to demonstrate the non-inferiority of MenACWY-TT (Lot A) when compared to Menactra at 10-25 years of age in terms of the percentage of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY vaccine response* one month after vaccination.</p> <p>*Vaccine response is defined as an hSBA titer of at least 1:8 in subjects initially seronegative (hSBA titer &lt;1:4) and as a 4-fold increase in titer in subjects initially seropositive (hSBA titer 1:4).</p> <p>In addition, to support the data obtained by hSBA testing, antibody concentrations against meningococcal polysaccharides were planned to be assessed by ELISA. The sponsor decided not to perform the ELISA testing for the following reasons:</p> <ul style="list-style-type: none"><li>• the World Health Organisation (WHO) considers SBA the primary means of assessing immune response to meningococcal conjugate vaccines [WHO, 2006;WHO, 1999]</li><li>• circulating bactericidal antibodies are more critical for persistent protection against meningococcal disease than non-functional antibodies against meningococcal polysaccharides [CDC, 2011; WHO, 2006].</li></ul> <p>Section 6.2 (Storage and handling of study vaccines) has been modified in order to align the wording with the new version of SOP-BIO-CLIN-7055 v04 entitled "Management of the Cold Chain for GlaxoSmithKline Biologicals investigational human subject research" effective since 31 March 2010.</p> |
| 06 September 2010 | <ul style="list-style-type: none"><li>• The MenA capsular polysaccharide O-acetylation in MenACWY-TT vaccine Lot A will be 68% instead of 61%.</li><li>• Mencevax™ ACWY is not licensed in Canada.</li><li>• Menveo® (Novartis' meningococcal [groups A, C, Y and W-135] oligosaccharide diphtheria CRM197 conjugate vaccine) was recently licensed in Canada.</li><li>• A new abbreviation was added to the List of Abbreviations.</li><li>• For clarification, the word "days" was added after "180-210" in Table 3 Intervals between study visits.</li><li>• For clarification, the 31-day post-vaccination reporting period for pregnancies was added to Figure 1.</li><li>• New safety reporting telephone numbers replaced the old numbers.</li></ul> <p>New study contact for emergency code break telephone numbers replaced the old numbers.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported