



Clinical trial results:

A phase III, randomized, controlled, single-blind study to evaluate the non-inferiority of GlaxoSmithKline Biologicals' 10-valent pneumococcal conjugate vaccine compared to the 7-valent pneumococcal conjugate vaccine Prevenar™ when administered as a 3-dose primary immunization course at 2, 4 and 6 months of age, co-administered with GSK Biologicals' Hiberix™ vaccine.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2015-001505-14 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 08 May 2009 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 |
| This version publication date | 01 April 2016 |
| First version publication date | 25 July 2015 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 110808 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00680914 |
| 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 | 31 August 2009 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 08 May 2009 |
| Global end of trial reached? | Yes |
| Global end of trial date | 08 May 2009 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that GSK Biologicals' 10-valent pneumococcal conjugate vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar for the immune response against at least 7 of the pneumococcal serotypes contained in the 10-valent pneumococcal conjugate vaccine.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up for one month (minimum 30 days) following administration of the last dose of study vaccines.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 10 June 2008 |
| 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 | Korea, Republic of: 503 |
| Worldwide total number of subjects | 503 |
| 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) | 503 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |

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

Subject disposition

Recruitment

Recruitment details: -

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 | Overall Period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind |
| Roles blinded | Subject |

Blinding implementation details:

This study was conducted in a single-blind manner meaning that the investigator and/or his staff were aware of the treatment assignment but the subjects parent(s)/guardian(s) were not.

Arms

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

Arm description:

Subjects received 3 doses of Synflorix vaccine co-administered with Hiberix vaccine at Study Months 0, 2 and 4.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Pneumococcal vaccine GSK1024850A (Synflorix) |
| Investigational medicinal product code | |
| Other name | 10Pn-PD-DiT |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3 doses administered intramuscularly.

| | |
|--|---|
| Investigational medicinal product name | GSK Biologicals' Hiberix™ |
| Investigational medicinal product code | |
| Other name | Hib |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3 doses administered intramuscularly.

| | |
|------------------|----------------|
| Arm title | Prevenar Group |
|------------------|----------------|

Arm description:

Subjects received 3 doses of Prevenar vaccine co-administered with Hiberix vaccine at Study Months 0, 2 and 4.

| | |
|--|---|
| Arm type | Active comparator |
| Investigational medicinal product name | GSK Biologicals' Hiberix™ |
| Investigational medicinal product code | |
| Other name | Hib |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3 doses administered intramuscularly.

| | |
|--|--------------------------|
| Investigational medicinal product name | Prevenar |
| Investigational medicinal product code | |
| Other name | 7Pn |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3 doses administered intramuscularly.

| Number of subjects in period 1 | Synflorix Group | Prevenar Group |
|---------------------------------------|-----------------|----------------|
| Started | 374 | 129 |
| Completed | 364 | 125 |
| Not completed | 10 | 4 |
| Adverse event, serious fatal | - | 1 |
| Consent withdrawn by subject | 6 | 3 |
| Lost to follow-up | 4 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | Synflorix Group |
|-----------------------|-----------------|

Reporting group description:

Subjects received 3 doses of Synflorix vaccine co-administered with Hiberix vaccine at Study Months 0, 2 and 4.

| | |
|-----------------------|----------------|
| Reporting group title | Prevenar Group |
|-----------------------|----------------|

Reporting group description:

Subjects received 3 doses of Prevenar vaccine co-administered with Hiberix vaccine at Study Months 0, 2 and 4.

| Reporting group values | Synflorix Group | Prevenar Group | Total |
|--|-----------------|----------------|-------|
| Number of subjects | 374 | 129 | 503 |
| 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: weeks | | | |
| arithmetic mean | 9.5 | 9.5 | |
| standard deviation | ± 1.49 | ± 1.43 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 189 | 71 | 260 |
| Male | 185 | 58 | 243 |

End points

End points reporting groups

| | |
|---|-----------------|
| Reporting group title | Synflorix Group |
| Reporting group description: Subjects received 3 doses of Synflorix vaccine co-administered with Hiberix vaccine at Study Months 0, 2 and 4. | |
| Reporting group title | Prevenar Group |
| Reporting group description: Subjects received 3 doses of Prevenar vaccine co-administered with Hiberix vaccine at Study Months 0, 2 and 4. | |

Primary: Number of Subjects With Vaccine Pneumococcal Serotypes Antibody Concentrations Above the Cut-Off Value

| | |
|--|--|
| End point title | Number of Subjects With Vaccine Pneumococcal Serotypes Antibody Concentrations Above the Cut-Off Value |
| End point description: Anti-pneumococcal antibody cut-off value assessed was 0.20 microgram per milliliter (ug/mL). The vaccine pneumococcal serotypes assessed include 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F. | |
| End point type | Primary |
| End point timeframe: One month after administration of 3rd dose of the pneumococcal conjugate vaccine | |

| End point values | Synflorix Group | Prevenar Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 344 | 123 | | |
| Units: Subjects | | | | |
| Anti-1 | 344 | 7 | | |
| Anti-4 | 343 | 123 | | |
| Anti-5 | 344 | 18 | | |
| Anti-6B | 318 | 121 | | |
| Anti-7F | 344 | 4 | | |
| Anti-9V | 343 | 122 | | |
| Anti-14 | 342 | 123 | | |
| Anti-18C | 343 | 123 | | |
| Anti-19F | 340 | 123 | | |
| Anti-23F | 331 | 121 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Immune response non-inferiority–Anti-4 |
| Statistical analysis description: To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the | |

pneumococcal serotypes contained in the GSK 1024850A vaccine.

| | |
|---|----------------------------------|
| Comparison groups | Synflorix Group v Prevenar Group |
| Number of subjects included in analysis | 467 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[1] |
| Parameter estimate | Difference in percentage |
| Point estimate | 0.29 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.21 |
| upper limit | 1.81 |

Notes:

[1] - For each of the Prevenar™ vaccine serotypes, non-inferiority was demonstrated if the upper limit of the 2-sided 96.5% confidence interval (CI) (adjusted 1-sided alpha = 0.0175) of the difference between groups (Prevenar Group minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥ 0.2 mg/mL, was lower than 10%.

| | |
|-----------------------------------|--|
| Statistical analysis title | Immune response non-inferiority –Anti-6B |
|-----------------------------------|--|

Statistical analysis description:

To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the pneumococcal serotypes contained in the GSK 1024850A vaccine.

| | |
|---|----------------------------------|
| Comparison groups | Synflorix Group v Prevenar Group |
| Number of subjects included in analysis | 467 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[2] |
| Parameter estimate | Difference in percentage |
| Point estimate | 5.93 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.92 |
| upper limit | 9.86 |

Notes:

[2] - For each of the Prevenar™ vaccine serotypes, non-inferiority was demonstrated if the upper limit of the 2-sided 96.5% confidence interval (CI) (adjusted 1-sided alpha = 0.0175) of the difference between groups (Prevenar Group minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥ 0.2 mg/mL, was lower than 10%.

| | |
|-----------------------------------|--|
| Statistical analysis title | Immune response non-inferiority –Anti-9V |
|-----------------------------------|--|

Statistical analysis description:

To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the pneumococcal serotypes contained in the GSK 1024850A vaccine.

| | |
|---|----------------------------------|
| Comparison groups | Synflorix Group v Prevenar Group |
| Number of subjects included in analysis | 467 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[3] |
| Parameter estimate | Difference in percentage |
| Point estimate | -0.52 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.66 |
| upper limit | 1.1 |

Notes:

[3] - For each of the Prevenar™ vaccine serotypes, non-inferiority was demonstrated if the upper limit of the 2-sided 96.5% confidence interval (CI) (adjusted 1-sided alpha = 0.0175) of the difference between groups (Prevenar Group minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥ 0.2 mg/mL, was lower than 10%.

| | |
|-----------------------------------|--|
| Statistical analysis title | Immune response non-inferiority –Anti-14 |
|-----------------------------------|--|

Statistical analysis description:

To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the pneumococcal serotypes contained in the GSK 1024850A vaccine.

| | |
|---|----------------------------------|
| Comparison groups | Synflorix Group v Prevenar Group |
| Number of subjects included in analysis | 467 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[4] |
| Parameter estimate | Difference in percentage |
| Point estimate | 0.58 |

Confidence interval

| | |
|-------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.92 |
| upper limit | 2.28 |

Notes:

[4] - For each of the Prevenar™ vaccine serotypes, non-inferiority was demonstrated if the upper limit of the 2-sided 96.5% confidence interval (CI) (adjusted 1-sided alpha = 0.0175) of the difference between groups (Prevenar Group minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥ 0.2 mg/mL, was lower than 10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | Immune response non-inferiority –Anti-18C |
|-----------------------------------|---|

Statistical analysis description:

To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the pneumococcal serotypes contained in the GSK 1024850A vaccine.

| | |
|---|----------------------------------|
| Comparison groups | Synflorix Group v Prevenar Group |
| Number of subjects included in analysis | 467 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[5] |
| Parameter estimate | Difference in percentage |
| Point estimate | 0.29 |

Confidence interval

| | |
|-------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.21 |
| upper limit | 1.81 |

Notes:

[5] - For each of the Prevenar™ vaccine serotypes, non-inferiority was demonstrated if the upper limit of the 2-sided 96.5% confidence interval (CI) (adjusted 1-sided alpha = 0.0175) of the difference between groups (Prevenar Group minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥ 0.2 mg/mL, was lower than 10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | Immune response non-inferiority –Anti-19F |
|-----------------------------------|---|

Statistical analysis description:

To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the pneumococcal serotypes contained in the GSK 1024850A vaccine.

| | |
|---|----------------------------------|
| Comparison groups | Synflorix Group v Prevenar Group |
| Number of subjects included in analysis | 467 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[6] |
| Parameter estimate | Difference in percentage |
| Point estimate | 1.16 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.34 |
| upper limit | 3.15 |

Notes:

[6] - For each of the Prevenar™ vaccine serotypes, non-inferiority was demonstrated if the upper limit of the 2-sided 96.5% confidence interval (CI) (adjusted 1-sided alpha = 0.0175) of the difference between groups (Prevenar Group minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥ 0.2 mg/mL, was lower than 10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | Immune response non-inferiority –Anti-23F |
|-----------------------------------|---|

Statistical analysis description:

To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the pneumococcal serotypes contained in the GSK 1024850A vaccine.

| | |
|---|----------------------------------|
| Comparison groups | Synflorix Group v Prevenar Group |
| Number of subjects included in analysis | 467 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[7] |
| Parameter estimate | Difference in percentage |
| Point estimate | 2.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.65 |
| upper limit | 5.34 |

Notes:

[7] - For each of the Prevenar™ vaccine serotypes, non-inferiority was demonstrated if the upper limit of the 2-sided 96.5% confidence interval (CI) (adjusted 1-sided alpha = 0.0175) of the difference between groups (Prevenar Group minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥ 0.2 mg/mL, was lower than 10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | Immune response non-inferiority –Anti-1 |
|-----------------------------------|---|

Statistical analysis description:

To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the pneumococcal serotypes contained in the GSK 1024850A vaccine.

| | |
|---|----------------------------------|
| Comparison groups | Synflorix Group v Prevenar Group |
| Number of subjects included in analysis | 467 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[8] |
| Parameter estimate | Difference in percentage |
| Point estimate | -0.58 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.95 |
| upper limit | 0.18 |

Notes:

[8] - For each of the 3 non-Prevenar™ vaccine serotypes (i.e., 1, 5 and 7F), non-inferiority was demonstrated if the upper limit of the 96.5% CI of the difference between the aggregate response for the Prevenar™ vaccine serotypes and responses to 1, 5 and 7F in Synflorix Group, (Aggregate 7Pn [=number of subjects in the Prevenar Group, multiplied by 7] minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥ 0.2 mg/mL, was lower than 10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | Immune response non-inferiority –Anti-5 |
|-----------------------------------|---|

Statistical analysis description:

To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the pneumococcal serotypes contained in the GSK 1024850A vaccine.

| | |
|---|----------------------------------|
| Comparison groups | Synflorix Group v Prevenar Group |
| Number of subjects included in analysis | 467 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[9] |
| Parameter estimate | Difference in percentage |
| Point estimate | -0.58 |

Confidence interval

| | |
|-------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.95 |
| upper limit | 0.18 |

Notes:

[9] - For each of the 3 non-Prevenar™ vaccine serotypes (i.e., 1, 5 and 7F), non-inferiority was demonstrated if the upper limit of the 96.5% CI of the difference between the aggregate response for the Prevenar™ vaccine serotypes and responses to 1, 5 and 7F in Synflorix Group, (Aggregate 7Pn [=number of subjects in the Prevenar Group, multiplied by 7] minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥ 0.2 mg/mL, was lower than 10%.

| | |
|-----------------------------------|--|
| Statistical analysis title | Immune response non-inferiority –Anti-7F |
|-----------------------------------|--|

Statistical analysis description:

To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the pneumococcal serotypes contained in the GSK 1024850A vaccine.

| | |
|---|----------------------------------|
| Comparison groups | Synflorix Group v Prevenar Group |
| Number of subjects included in analysis | 467 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[10] |
| Parameter estimate | Difference in percentage |
| Point estimate | -0.58 |

Confidence interval

| | |
|-------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.95 |
| upper limit | 0.18 |

Notes:

[10] - For each of the 3 non-Prevenar™ vaccine serotypes (i.e., 1, 5 and 7F), non-inferiority was demonstrated if the upper limit of the 96.5% CI of the difference between the aggregate response for the Prevenar™ vaccine serotypes and responses to 1, 5 and 7F in Synflorix Group, (Aggregate 7Pn [=number of subjects in the Prevenar Group, multiplied by 7] minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥ 0.2 mg/mL, was lower than 10%.

Secondary: Number of subjects with a seropositivity status against protein D and defined pneumococcal serotypes

| | |
|-----------------|--|
| End point title | Number of subjects with a seropositivity status against protein D and defined pneumococcal serotypes |
|-----------------|--|

End point description:

Seropositivity status for protein D is defined as anti protein D (anti-PD) antibody concentrations ≥ 100 Enzyme-Linked Immuno Sorbent Assay (EL) units EL.U/mL. Seropositivity status for pneumococcal serotypes is defined as anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations ≥ 0.05 ug/mL.

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

End point timeframe:

One month after the administration of the 3rd vaccine dose of the pneumococcal conjugate vaccine

| End point values | Synflorix Group | Prevenar Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 344 | 123 | | |
| Units: Subjects | | | | |
| Anti-PD | 343 | 123 | | |
| Anti-1 | 344 | 44 | | |
| Anti-4 | 344 | 123 | | |
| Anti-5 | 344 | 85 | | |
| Anti-6B | 337 | 122 | | |
| Anti-7F | 344 | 22 | | |
| Anti-9V | 343 | 123 | | |
| Anti-14 | 344 | 123 | | |
| Anti-18C | 344 | 123 | | |
| Anti-19F | 344 | 123 | | |
| Anti-23F | 340 | 122 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with opsonophagocytic activity against pneumococcal serotypes contained in the vaccine above the cut-off value

| | |
|-----------------|---|
| End point title | Number of subjects with opsonophagocytic activity against pneumococcal serotypes contained in the vaccine above the cut-off value |
|-----------------|---|

End point description:

The results were presented as the dilution of serum (opsonic titer) able to sustain 50% killing of live pneumococci under the assay conditions. In this assay the cut-off value for opsonophagocytic activity against pneumococcal antibody assessed was ≥ 8 . The vaccine pneumococcal serotypes assessed include 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F.

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

End point timeframe:

One month after the administration of the 3rd vaccine dose of the pneumococcal conjugate vaccine

| End point values | Synflorix Group | Prevenar Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 165 | 63 | | |
| Units: Subjects | | | | |
| Opsono-1 (N=162; 62) | 150 | 8 | | |
| Opsono-4 (N=161; 63) | 158 | 63 | | |
| Opsono-5 (N=165; 62) | 161 | 6 | | |
| Opsono-6B (N=162; 63) | 152 | 63 | | |
| Opsono-7F (N=164; 59) | 164 | 40 | | |
| Opsono-9V (N= 165; 63) | 164 | 62 | | |
| Opsono-14 (N= 165; 63) | 163 | 62 | | |
| Opsono-18C (N= 159; 63) | 142 | 61 | | |
| Opsono-19F (N=164; 61) | 159 | 55 | | |
| Opsono-23F (N= 164; 63) | 160 | 62 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With cross-reactive Pneumococcal Serotype Antibody Concentrations Above the Cut-Off Value

| | |
|-----------------|--|
| End point title | Number of Subjects With cross-reactive Pneumococcal Serotype Antibody Concentrations Above the Cut-Off Value |
|-----------------|--|

End point description:

Anti-pneumococcal antibody cut-off value assessed was 0.20 microgram per milliliter (ug/mL).
Pneumococcal cross-reactive serotypes were 6A and 19A.

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

End point timeframe:

One month after the administration of the 3rd vaccine dose of the pneumococcal conjugate vaccine

| End point values | Synflorix Group | Prevenar Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 344 | 123 | | |
| Units: Subjects | | | | |
| Anti-6A | 232 | 85 | | |
| Anti-19A | 203 | 33 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against Pneumococcal serotypes contained in the vaccine

| | |
|-----------------|---|
| End point title | Antibody concentrations against Pneumococcal serotypes contained in the vaccine |
|-----------------|---|

End point description:

Concentrations are reported as Geometric Mean Concentrations in ug/mL. Pneumococcal serotypes assessed include 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F.

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

End point timeframe:

One month after the administration of the 3rd vaccine dose of the pneumococcal conjugate vaccine

| End point values | Synflorix Group | Prevenar Group | | |
|--|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 344 | 123 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-1 | 3.41 (3.14 to 3.71) | 0.04 (0.04 to 0.05) | | |
| Anti-4 | 4 (3.67 to 4.35) | 5.35 (4.66 to 6.15) | | |
| Anti-5 | 4.52 (4.24 to 4.83) | 0.07 (0.06 to 0.08) | | |
| Anti-6B | 1.4 (1.24 to 1.58) | 2.07 (1.75 to 2.44) | | |
| Anti-7F | 4.08 (3.77 to 4.41) | 0.03 (0.03 to 0.04) | | |
| Anti-9V | 3.39 (3.09 to 3.71) | 5.09 (4.34 to 5.96) | | |
| Anti-14 | 5.54 (5.02 to 6.12) | 8.51 (7.27 to 9.95) | | |
| Anti-18C | 5.8 (5.17 to 6.52) | 5.13 (4.31 to 6.11) | | |
| Anti-19F | 7.41 (6.67 to 8.23) | 2.77 (2.45 to 3.13) | | |
| Anti-23F | 1.96 (1.75 to 2.19) | 3.94 (3.26 to 4.77) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PD Antibody Concentration

| | |
|-----------------|--------------------------------|
| End point title | Anti-PD Antibody Concentration |
|-----------------|--------------------------------|

End point description:

Concentration of anti-PD antibody given as GMC expressed in EL.U/mL.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| One month after administration of 3rd vaccine dose of the pneumococcal conjugate vaccine | |

| End point values | Synflorix Group | Prevenar Group | | |
|--|-------------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 344 | 123 | | |
| Units: EL.U/mL. | | | | |
| geometric mean (confidence interval 95%) | 1622.4 (1500.8 to 1754) | 88.2 (74.7 to 104) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal cross-reactive serotypes

| | |
|--|---|
| End point title | Antibody concentrations against pneumococcal cross-reactive serotypes |
| End point description: | |
| Concentration of cross-reactive pneumococcal serotypes 6A and 19A in ug/mL. | |
| End point type | Secondary |
| End point timeframe: | |
| One month after the administration of the 3rd vaccine dose of the pneumococcal conjugate vaccine | |

| End point values | Synflorix Group | Prevenar Group | | |
|--|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 344 | 123 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-6A | 0.38 (0.33 to 0.44) | 0.48 (0.36 to 0.63) | | |
| Anti-19A | 0.29 (0.25 to 0.33) | 0.12 (0.1 to 0.14) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Opsonophagocytic activity against pneumococcal cross-reactive serotypes

| | |
|--|---|
| End point title | Number of subjects with Opsonophagocytic activity against pneumococcal cross-reactive serotypes |
| End point description: The results were presented as the dilution of serum (opsonic titer) able to sustain 50% killing of live pneumococci under the assay conditions. In this assay the cut-off value for opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A was defined as ≥ 8 . | |
| End point type | Secondary |
| End point timeframe: One month after the administration of the 3rd vaccine dose of the pneumococcal conjugate vaccine | |

| End point values | Synflorix Group | Prevenar Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 162 | 60 | | |
| Units: Subjects | | | | |
| Opsono-6A (N=158; 60) | 134 | 54 | | |
| Opsono-19A (N= 162; 60) | 53 | 7 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentrations

| | |
|--|---|
| End point title | Anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentrations |
| End point description: Concentration of anti-PRP antibody given as GMC in ug/mL. | |
| End point type | Secondary |
| End point timeframe: One month after the administration of the 3rd vaccine dose of the pneumococcal conjugate vaccine | |

| End point values | Synflorix Group | Prevenar Group | | |
|--|---------------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 60 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | 20.131 (16.775 to 24.158) | 11.844 (8.542 to 16.424) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Seroprotection status against PRP

| | |
|-----------------|---|
| End point title | Number of subjects with Seroprotection status against PRP |
|-----------------|---|

End point description:

Seroprotection status is defined as anti-PRP antibody concentrations above 0.15 ug/mL and above 1.0 ug/mL

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

End point timeframe:

One month after the administration of the 3rd vaccine dose of the pneumococcal conjugate vaccine

| End point values | Synflorix Group | Prevenar Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 60 | | |
| Units: Subjects | | | | |
| Above 0.15 | 175 | 60 | | |
| Above 1.0 | 173 | 58 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local symptoms

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

End point description:

Solicited local symptoms assessed include pain, redness and swelling.

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

End point timeframe:

Within 4 days after each vaccination

| End point values | Synflorix Group | Prevenar Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 371 | 129 | | |
| Units: Subjects | | | | |
| Pain | 210 | 72 | | |
| Redness | 252 | 84 | | |
| Swelling | 182 | 69 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms

| | |
|-----------------|--|
| End point title | Number of subjects with solicited general symptoms |
|-----------------|--|

End point description:

Solicited general symptoms assessed include drowsiness, fever, irritability and loss of appetite. Fever was defined as axillary temperature ≥ 37.5 degrees Celsius.

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

End point timeframe:

Within 4 days after each vaccination

| End point values | Synflorix Group | Prevenar Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 371 | 129 | | |
| Units: Subjects | | | | |
| Drowsiness | 212 | 65 | | |
| Fever | 113 | 33 | | |
| Irritability | 293 | 99 | | |
| Loss of Appetite | 177 | 66 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited adverse events

| | |
|-----------------|---|
| End point title | Number of subjects reporting unsolicited adverse events |
|-----------------|---|

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. Grade 3 AE = an AE which prevented normal, everyday activities. Related = AE assessed by the investigator as related to the vaccination.

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

End point timeframe:

Within 31 days after each vaccination

| End point values | Synflorix Group | Prevenar Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 374 | 129 | | |
| Units: Subjects | 213 | 62 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAE)

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

End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above.

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

End point timeframe:

Following the administration of the first dose of the study vaccines throughout the entire study period up to study month 5

| End point values | Synflorix Group | Prevenar Group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 374 | 129 | | |
| Units: Subjects | 56 | 9 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to study Month 5

Adverse event reporting additional description:

Analysis was performed on the Total Vaccinated Cohort, on subjects with available data. The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 12.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | Synflorix Group |
|-----------------------|-----------------|

Reporting group description:

Subjects received 3 doses of Synflorix vaccine co-administered with Hiberix vaccine at Study Months 0, 2 and 4

| | |
|-----------------------|----------------|
| Reporting group title | Prevenar Group |
|-----------------------|----------------|

Reporting group description:

Subjects received 3 doses of Prevenar vaccine co-administered with Hiberix vaccine at Study Months 0, 2 and 4

| Serious adverse events | Synflorix Group | Prevenar Group | |
|--|-------------------|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 56 / 374 (14.97%) | 9 / 129 (6.98%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Nervous system disorders | | | |
| Febrile convulsion | | | |
| subjects affected / exposed | 0 / 374 (0.00%) | 1 / 129 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 374 (0.53%) | 0 / 129 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Intussusception | | | |

| | | | |
|---|------------------|-----------------|--|
| subjects affected / exposed | 2 / 374 (0.53%) | 1 / 129 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enteritis | | | |
| subjects affected / exposed | 1 / 374 (0.27%) | 1 / 129 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Hepatitis | | | |
| subjects affected / exposed | 1 / 374 (0.27%) | 0 / 129 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Hydronephrosis | | | |
| subjects affected / exposed | 2 / 374 (0.53%) | 0 / 129 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Bronchiolitis | | | |
| subjects affected / exposed | 22 / 374 (5.88%) | 1 / 129 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 22 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 8 / 374 (2.14%) | 3 / 129 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 9 / 374 (2.41%) | 1 / 129 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 4 / 374 (1.07%) | 1 / 129 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Croup infections | | | |
| subjects affected / exposed | 2 / 374 (0.53%) | 1 / 129 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningitis aseptic | | | |
| subjects affected / exposed | 2 / 374 (0.53%) | 1 / 129 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngitis | | | |
| subjects affected / exposed | 3 / 374 (0.80%) | 0 / 129 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchopneumonia | | | |
| subjects affected / exposed | 2 / 374 (0.53%) | 0 / 129 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis rotavirus | | | |
| subjects affected / exposed | 2 / 374 (0.53%) | 0 / 129 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 2 / 374 (0.53%) | 0 / 129 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis media acute | | | |
| subjects affected / exposed | 2 / 374 (0.53%) | 0 / 129 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystitis | | | |
| subjects affected / exposed | 1 / 374 (0.27%) | 0 / 129 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Exanthema subitum | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 374 (0.27%) | 0 / 129 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpangina | | | |
| subjects affected / exposed | 1 / 374 (0.27%) | 0 / 129 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injection site abscess | | | |
| subjects affected / exposed | 1 / 374 (0.27%) | 0 / 129 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngitis | | | |
| subjects affected / exposed | 1 / 374 (0.27%) | 1 / 129 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningitis | | | |
| subjects affected / exposed | 1 / 374 (0.27%) | 0 / 129 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 374 (0.27%) | 0 / 129 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis media | | | |
| subjects affected / exposed | 1 / 374 (0.27%) | 0 / 129 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 1 / 374 (0.27%) | 0 / 129 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus bronchiolitis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 374 (0.00%) | 1 / 129 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 374 (0.00%) | 1 / 129 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 374 (0.00%) | 1 / 129 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Anorexia | | | |
| subjects affected / exposed | 0 / 374 (0.00%) | 1 / 129 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Synflorix Group | Prevenar Group | |
|---|--------------------|-------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 293 / 374 (78.34%) | 99 / 129 (76.74%) | |
| General disorders and administration site conditions | | | |
| Pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 210 / 374 (56.15%) | 72 / 129 (55.81%) | |
| occurrences (all) | 210 | 72 | |
| Redness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 252 / 374 (67.38%) | 84 / 129 (65.12%) | |
| occurrences (all) | 252 | 84 | |
| Swelling | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|--|--------------------|-------------------|--|
| subjects affected / exposed | 182 / 374 (48.66%) | 69 / 129 (53.49%) | |
| occurrences (all) | 182 | 69 | |
| Drowsiness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 212 / 374 (56.68%) | 65 / 129 (50.39%) | |
| occurrences (all) | 212 | 65 | |
| Fever | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 113 / 374 (30.21%) | 33 / 129 (25.58%) | |
| occurrences (all) | 113 | 33 | |
| Irritability | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 293 / 374 (78.34%) | 99 / 129 (76.74%) | |
| occurrences (all) | 293 | 99 | |
| Loss of appetite | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 177 / 374 (47.33%) | 66 / 129 (51.16%) | |
| occurrences (all) | 177 | 66 | |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 44 / 374 (11.76%) | 16 / 129 (12.40%) | |
| occurrences (all) | 44 | 16 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 42 / 374 (11.23%) | 16 / 129 (12.40%) | |
| occurrences (all) | 42 | 16 | |
| Bronchiolitis | | | |
| subjects affected / exposed | 20 / 374 (5.35%) | 4 / 129 (3.10%) | |
| occurrences (all) | 20 | 4 | |
| Pharyngitis | | | |
| subjects affected / exposed | 23 / 374 (6.15%) | 6 / 129 (4.65%) | |
| occurrences (all) | 23 | 6 | |
| Bronchitis | | | |
| subjects affected / exposed | 14 / 374 (3.74%) | 7 / 129 (5.43%) | |
| occurrences (all) | 14 | 7 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 11 February 2008 | The protocol has been amended according to comments received from the Korean FDA. In addition, the Detailed Study Title has been corrected. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported