



Clinical trial results:

Immunogenicity and Safety Study of a Booster Dose of DTaP-IPV-Hep B-PRP-T Combined Vaccine at 15 to 18 Months of Age Following a Primary Series at 2, 3 and 4 Months of Age in Healthy Turkish Infants.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2011-004432-58 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 07 July 2008 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 10 February 2016 |
| First version publication date | 31 July 2014 |

Trial information

Trial identification

| | |
|-----------------------|-------|
| Sponsor protocol code | A3L22 |
|-----------------------|-------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00619502 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Sanofi Pasteur, SA |
| Sponsor organisation address | 1541, Avenue Marcel Mérieux, Marcy L'Etoile, France, 69280 |
| Public contact | Director, Clinical Development, Sanofi Pasteur SA, 33 (0)4 37 37 58 43 , emmanuel.feroldi@sanofipasteur.com |
| Scientific contact | Director, Clinical Development, Sanofi Pasteur SA, 33 (0)4 37 37 58 43 , emmanuel.feroldi@sanofipasteur.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-001201-PIP01-11 |
| 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 | 02 March 2009 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 07 July 2008 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Immunogenicity

- To describe the antibody (Ab) persistence at 15 to 18 months of age for all valences following a three-dose primary series vaccination of either DTaP-IPV-Hep B-PRP-T or Pentaxim™ + Engerix™ B at 2, 3, and 4 months of age
- To describe the immunogenicity of a booster dose of DTaP-IPV-Hep B-PRP-T given at 15 to 18 months of age

Safety

- To describe the safety profile after a booster dose of DTaP-IPV-Hep B-PRP-T given at 15 to 18 months of age

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were randomized and vaccinated in the study. Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety.

Background therapy:

This is a booster vaccination study in toddlers who completed a three dose primary series of DTaP-IPV-Hep B-PRP-T combined vaccine or of Pentaxim™ + Engerix™ B in Study A3L10. All subjects were to receive the DTaP-IPV-Hep B-PRP-T vaccine as a booster dose.

Evidence for comparator:

Not applicable.

| | |
|---|------------------|
| Actual start date of recruitment | 14 December 2007 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Turkey: 254 |
| Worldwide total number of subjects | 254 |
| EEA total number of subjects | 0 |

Notes:

Subjects enrolled per age group

| | |
|--|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 | 0 |

| | |
|--|-----|
| wk | |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 254 |
| 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:

Participants were enrolled from 14 December 2007 to 07 January 2008 at 1 clinical center in Turkey.

Pre-assignment

Screening details:

Only subjects who met all inclusion, but none of the exclusion criteria were enrolled and vaccinated

Period 1

| | |
|------------------------------|---------------------------------------|
| Period 1 title | Overall Study Period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Blinding implementation details:

Not Applicable.

Arms

| | |
|------------------------------|---------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | DTaP-IPV-HepB-PRP~T |

Arm description:

All participants received a primary series of 3 vaccinations with DTaP-IPV-HepB-PRP~T, with 1 dose each at 2, 3, and 4 months of age, in Study A3L10; they received a booster dose of DTaP-IPV-HepB-PRP~T at 15 to 18 months of age in the present study.

| | |
|--|-----------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Hexaxim |
| Investigational medicinal product code | DTaP-IPV-HepB-PRP-T vaccine |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL, Intramuscular injection into the right deltoid muscle.

| | |
|------------------|------------------------|
| Arm title | Pentaxim™ + Engerix B™ |
|------------------|------------------------|

Arm description:

All participants received a primary series of 3 vaccinations with Pentaxim™ and Engerix B™ vaccines, with 1 dose each at 2, 3, and 4 months of age, in Study A3L10; they received a booster dose of DTaP-IPV-Hep B-PRP~T at 15 to 18 months of age in the present study.

| | |
|--|-----------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Hexaxim |
| Investigational medicinal product code | DTaP-IPV-HepB-PRP-T vaccine |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL, Intramuscular injection into the right deltoid muscle.

| Number of subjects in period 1 | DTaP-IPV-HepB- PRP~T | Pentaxim™ + Engerix B™ |
|---------------------------------------|-------------------------|---------------------------|
| Started | 130 | 124 |
| Completed | 122 | 114 |
| Not completed | 8 | 10 |
| Lost to follow-up | 8 | 10 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------------|
| Reporting group title | DTaP-IPV-HepB-PRP~T |
|-----------------------|---------------------|

Reporting group description:

All participants received a primary series of 3 vaccinations with DTaP-IPV-HepB-PRP~T, with 1 dose each at 2, 3, and 4 months of age, in Study A3L10; they received a booster dose of DTaP-IPV-HepB-PRP~T at 15 to 18 months of age in the present study.

| | |
|-----------------------|------------------------|
| Reporting group title | Pentaxim™ + Engerix B™ |
|-----------------------|------------------------|

Reporting group description:

All participants received a primary series of 3 vaccinations with Pentaxim™ and Engerix B™ vaccines, with 1 dose each at 2, 3, and 4 months of age, in Study A3L10; they received a booster dose of DTaP-IPV-Hep B-PRP~T at 15 to 18 months of age in the present study.

| Reporting group values | DTaP-IPV-HepB-PRP~T | Pentaxim™ + Engerix B™ | Total |
|--|---------------------|------------------------|-------|
| Number of subjects | 130 | 124 | 254 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 130 | 124 | 254 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Units: months | | | |
| arithmetic mean | 17.6 | 17.6 | |
| standard deviation | ± 0.198 | ± 0.279 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 56 | 54 | 110 |
| Male | 74 | 70 | 144 |

End points

End points reporting groups

| | |
|--|------------------------|
| Reporting group title | DTaP-IPV-HepB-PRP~T |
| Reporting group description: | |
| All participants received a primary series of 3 vaccinations with DTaP-IPV-HepB-PRP~T, with 1 dose each at 2, 3, and 4 months of age, in Study A3L10; they received a booster dose of DTaP-IPV-HepB-PRP~T at 15 to 18 months of age in the present study. | |
| Reporting group title | Pentaxim™ + Engerix B™ |
| Reporting group description: | |
| All participants received a primary series of 3 vaccinations with Pentaxim™ and Engerix B™ vaccines, with 1 dose each at 2, 3, and 4 months of age, in Study A3L10; they received a booster dose of DTaP-IPV-Hep B-PRP~T at 15 to 18 months of age in the present study. | |

Primary: Percentage of Participants With Pre-booster Antibody Persistence and Booster Response to DTaP-IPV-Hep B-PRP~T After Primary Vaccination With Either DTaP-IPV-Hep B-PRP~T or Pentaxim™ + Engerix B Vaccine™

| | |
|---|---|
| End point title | Percentage of Participants With Pre-booster Antibody Persistence and Booster Response to DTaP-IPV-Hep B-PRP~T After Primary Vaccination With Either DTaP-IPV-Hep B-PRP~T or Pentaxim™ + Engerix B Vaccine™ ^[1] |
| End point description: | |
| Antibody titers measured by chemiluminescence detection for Hepatitis B (Hep B); Farr type radioimmunoassay for Haemophilus influenza type b (PRP); toxin neutralization for Diphtheria (D); indirect enzyme-linked immunosorbent assay (ELISA) for Tetanus (T); neutralization assay for Poliovirus types 1, 2, and 3; and ELISA for Pertussis toxoid (PT) and Filamentous hemagglutinin (FHA). Persistence and response: ≥ 10 mIU/mL for anti-Hep B, ≥ 0.15 µg/mL for anti-PRP, ≥ 0.01 IU/mL for anti-D and anti-T, ≥ 8 (1/dil) for anti-Poliovirus; and ≥ 4-fold increase from Day 0 for anti-PT and anti-FHA. | |
| End point type | Primary |
| End point timeframe: | |
| Day 0 before and Day 30 Post-booster 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: Descriptive analyses were performed, based on the vaccine groups from the primary series for the follow-up booster vaccination in this study.

| End point values | DTaP-IPV-HepB-PRP~T | Pentaxim™ + Engerix B™ | | |
|------------------------------|---------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 114 | 103 | | |
| Units: Percentage | | | | |
| Anti-FHA Post-booster | 92 | 97 | | |
| Anti-PT Post-booster | 97 | 96 | | |
| Anti-Polio 3 Post-booster | 100 | 100 | | |
| Anti-Polio 3 Pre-booster | 85 | 97 | | |
| Anti-Polio 2 Post-booster | 100 | 100 | | |
| Anti-Polio 2 Pre-booster | 100 | 98 | | |
| Anti-Polio 1 Post-booster | 100 | 100 | | |
| Anti-Polio 1 Pre-booster | 99 | 99 | | |
| Anti-Tetanus Post-booster | 100 | 100 | | |
| Anti-Tetanus Pre-booster | 100 | 100 | | |
| Anti-Diphtheria Post-booster | 100 | 100 | | |

| | | | | |
|-----------------------------|-----|-----|--|--|
| Anti-Diphtheria Pre-booster | 90 | 88 | | |
| Anti-PRP Post-booster | 100 | 100 | | |
| Anti-PRP Pre-booster | 85 | 83 | | |
| Anti-Hep B Post-booster | 97 | 100 | | |
| Anti-Hep B Pre-booster | 81 | 99 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) Before and After Booster Vaccination With DTaP-IPV-Hep B-PRP~T

| | |
|-----------------|--|
| End point title | Geometric Mean Titers (GMTs) Before and After Booster Vaccination With DTaP-IPV-Hep B-PRP~T ^[2] |
|-----------------|--|

End point description:

Antibody titers were measured by chemiluminescence detection for Hepatitis B (Hep B); Farr type radioimmunoassay for Haemophilus influenza type b (PRP); toxin neutralization test for Diphtheria (D); indirect enzyme-linked immunosorbent assay (ELISA) for Tetanus (T); neutralization assay for Poliovirus types 1, 2, and 3; and ELISA for Pertussis toxoid (PT) and Filamentous hemagglutinin (FHA).

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

End point timeframe:

Day 0 before and Day 30 post-booster vaccine

Notes:

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

Justification: Descriptive analyses were performed, based on the vaccine groups from the primary series for the follow-up booster vaccination in this study.

| End point values | DTaP-IPV-HepB-PRP~T | Pentaxim™ + Engerix B™ | | |
|--|---------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 114 | 103 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-FHA Post-booster | 222 (194 to 254) | 234 (201 to 272) | | |
| Anti-FHA Pre-booster | 12.5 (9.59 to 16.4) | 8.18 (6.49 to 10.3) | | |
| Anti-PT Post-booster | 160 (137 to 187) | 237 (202 to 278) | | |
| Anti-PT Pre-booster | 6.08 (4.74 to 7.79) | 7.49 (5.97 to 9.41) | | |
| Anti-Polio 3 Post-booster | 5542 (4156 to 7392) | 10152 (7806 to 13205) | | |
| Anti-Polio 3 Pre-booster | 47.1 (33.1 to 67.1) | 101 (73 to 141) | | |
| Anti-Polio 2 Post-booster | 6099 (4916 to 7566) | 9170 (7170 to 11727) | | |
| Anti-Polio 2 Pre-booster | 114 (84.9 to 153) | 131 (95.3 to 179) | | |
| Anti-Polio 1 Post-booster | 5477 (4401 to 5814) | 9050 (7134 to 11480) | | |
| Anti-Polio 1 Pre-booster | 110 (81.6 to 148) | 114 (82.4 to 157) | | |

| | | | | |
|------------------------------|------------------------|------------------------|--|--|
| Anti-Tetanus Post-booster | 8.98 (7.52 to 10.7) | 13.1 (10.8 to 15.8) | | |
| Anti-Tetanus Pre-booster | 0.244 (0.204 to 0.292) | 0.194 (0.158 to 0.238) | | |
| Anti-Diphtheria Post-booster | 5.09 (3.89 to 6.66) | 10.2 (7.59 to 13.8) | | |
| Anti-Diphtheria Pre-booster | 0.028 (0.022 to 0.035) | 0.032 (0.024 to 0.041) | | |
| Anti-PRP Post-booster | 72.5 (55.8 to 94.3) | 86.9 (69.8 to 108) | | |
| Anti-PRP Pre-booster | 0.724 (0.541 to 0.968) | 0.612 (0.443 to 0.844) | | |
| Anti-Hep B Post-booster | 1379 (916 to 2078) | 26189 (19133 to 35846) | | |
| Anti-Hep B Pre-booster | 44.2 (32.3 to 60.7) | 223 (176 to 282) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Solicited Injection Site and Systemic Reactions After Booster Vaccination With DTaP-IPV-Hep B-PRP~T

| | |
|-----------------|--|
| End point title | Number of Participants With Solicited Injection Site and Systemic Reactions After Booster Vaccination With DTaP-IPV-Hep B-PRP~T ^[3] |
|-----------------|--|

End point description:

Solicited Injection Site Reactions: Pain, Erythema, Swelling, and Extensive Swelling of Vaccinated Limb. Solicited Systemic Reactions: Pyrexia (Temperature), Vomiting, Crying, Somnolence, Anorexia, and Irritability.

Grade 3 defined as: Pain, cries when injected limb is moved or movement of limb reduced; Erythema and Swelling, ≥ 5 cm; Extensive Swelling of Vaccinated Limb, All; Pyrexia, $\geq 39^{\circ}\text{C}$; Vomiting, ≥ 6 episodes/24 hours or requiring parenteral hydration; Crying > 3 hours; Somnolence, sleeping most of time or difficult to wake up; Anorexia, refuses ≥ 3 feeds or most feeds; Irritability, inconsolable.

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

End point timeframe:

Day 0 up to Day 7 post-booster vaccination

Notes:

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

Justification: Descriptive analyses were performed, based on the vaccine groups from the primary series for the follow-up booster vaccination in this study.

| End point values | DTaP-IPV-HepB-PRP~T | Pentaxim™ + Engerix B™ | | |
|---------------------------------------|---------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 121 | 111 | | |
| Units: Participants | | | | |
| Injection site Pain | 56 | 67 | | |
| Grade 3 injection site Pain | 4 | 2 | | |
| Injection site Erythema | 34 | 50 | | |
| Grade 3 Injection site Erythema | 3 | 4 | | |
| Injection site Swelling | 26 | 36 | | |
| Grade 3 Injection site Swelling | 2 | 3 | | |
| Extensive Swelling of vaccinated limb | 0 | 0 | | |

| | | | | |
|----------------------|----|----|--|--|
| Pyrexia | 29 | 36 | | |
| Grade 3 Pyrexia | 1 | 0 | | |
| Vomiting | 13 | 11 | | |
| Grade 3 Vomiting | 2 | 2 | | |
| Crying | 29 | 35 | | |
| Grade 3 Crying | 3 | 4 | | |
| Somnolence | 24 | 25 | | |
| Grade 3 Somnolence | 2 | 3 | | |
| Anorexia | 40 | 43 | | |
| Grade 3 Anorexia | 9 | 8 | | |
| Irritability | 51 | 61 | | |
| Grade 3 Irritability | 5 | 7 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events data were collected from Day 0 after booster vaccination to up to 6 months after vaccination.

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

Dictionary used

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

| | |
|--------------------|-----|
| Dictionary version | 9.0 |
|--------------------|-----|

Reporting groups

| | |
|-----------------------|---------------------|
| Reporting group title | DTaP-IPV-HepB-PRP~T |
|-----------------------|---------------------|

Reporting group description:

All participants received a primary series of 3 vaccinations with DTaP-IPV-HepB-PRP~T, with 1 dose each at 2, 3, and 4 months of age, in Study A3L10; they received a booster dose of DTaP-IPV-HepB-PRP~T at 15 to 18 months of age in the present study.

| | |
|-----------------------|------------------------|
| Reporting group title | Pentaxim™ + Engerix B™ |
|-----------------------|------------------------|

Reporting group description:

All participants received a primary series of 3 vaccinations with Pentaxim™ and Engerix B™ vaccines, with 1 dose each at 2, 3, and 4 months of age, in Study A3L10; they received a booster dose of DTaP-IPV-Hep B-PRP~T at 15 to 18 months of age in the present study.

| Serious adverse events | DTaP-IPV-HepB-PRP~T | Pentaxim™ + Engerix B™ | |
|---|---------------------|------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 130 (3.08%) | 2 / 122 (1.64%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Poisoning | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 122 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Gastroesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 122 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Bronchitis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 122 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 1 / 122 (0.82%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis rotavirus | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 122 (0.82%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | DTaP-IPV-HepB-PRP~T | Pentaxim™ + Engerix B™ | |
|---|---------------------|------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 56 / 130 (43.08%) | 67 / 122 (54.92%) | |
| Nervous system disorders | | | |
| Somnolence | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[1] | 24 / 121 (19.83%) | 25 / 111 (22.52%) | |
| occurrences (all) | 24 | 25 | |
| General disorders and administration site conditions | | | |
| Injection site erythema | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[2] | 35 / 121 (28.93%) | 50 / 111 (45.05%) | |
| occurrences (all) | 35 | 50 | |
| Injection site pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[3] | 56 / 121 (46.28%) | 67 / 111 (60.36%) | |
| occurrences (all) | 56 | 67 | |
| Injection site swelling | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|-------------------------|-------------------------|--|
| subjects affected / exposed ^[4] occurrences (all) | 26 / 121 (21.49%) 26 | 36 / 111 (32.43%) 36 | |
| Irritability alternative assessment type: Systematic subjects affected / exposed ^[5] occurrences (all) | 51 / 121 (42.15%) 51 | 61 / 111 (54.95%) 61 | |
| Pyrexia alternative assessment type: Systematic subjects affected / exposed ^[6] occurrences (all) | 29 / 121 (23.97%) 29 | 36 / 111 (32.43%) 36 | |
| Gastrointestinal disorders Vomiting alternative assessment type: Systematic subjects affected / exposed ^[7] occurrences (all) | 13 / 121 (10.74%) 13 | 11 / 111 (9.91%) 11 | |
| Psychiatric disorders Crying alternative assessment type: Systematic subjects affected / exposed ^[8] occurrences (all) | 29 / 121 (23.97%) 29 | 35 / 111 (31.53%) 35 | |
| Metabolism and nutrition disorders Anorexia alternative assessment type: Systematic subjects affected / exposed ^[9] occurrences (all) | 40 / 121 (33.06%) 40 | 43 / 111 (38.74%) 43 | |

Notes:

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

Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

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

Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

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

Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects

exposed for the reporting group. These numbers are expected to be equal.

Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

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

Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

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

Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

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

Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

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

Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

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

Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|---|
| 07 July 2008 | The protocol amendment of 04 August 2008 was due to changes in the Sanofi Pastuer Global Clinical Immunology (GCI) laboratory methodology. Originally it had been planned to subcontract from GCI the analysis of the PRP valence, using the Enzyme linked immunosorbent assay (ELISA). However, due to capacity problems at the subcontracted laboratory and in order to speed up the availability of these data, the decision was made to perform this assay at GCI (using radioimmunoassay). The updated protocol documented this change and provided further details of CGI test methodology. Other administrative changes were also made to reflect changes to the nomenclature of the investigational product since the last protocol update, and changes to study personnel. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported