



Clinical trial results:

Immunogenicity and Safety of the Aventis Pasteur DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™), Given as a Three-Dose Primary Vaccination at 6, 10, and 14 Weeks of Age and Followed by a Booster Dose at 18 to 19 Months of Age in Healthy Infants in South Africa. All Infants Receiving Hepatitis B Monovalent Vaccine at 6, 10 and 14 Weeks of Age.

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2015-005354-35 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 15 February 2008 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 09 June 2016 |
| First version publication date | 09 June 2016 |

Trial information

Trial identification

| | |
|-----------------------|-------|
| Sponsor protocol code | E2I43 |
|-----------------------|-------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00254969 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--------------------------------------------------------------------------------------------|
| Sponsor organisation name | Sanofi Pasteur SA |
| Sponsor organisation address | 2, avenue Pont Pasteur, Lyon cedex 07, France, F-69367 |
| Public contact | Medical Team Leader, Sanofi Pasteur SA, 33 4 37 65 67 99, Emmanuel.vidor@sanofipasteur.com |
| Scientific contact | Medical Team Leader, Sanofi Pasteur SA, 33 4 37 65 67 99, Emmanuel.vidor@sanofipasteur.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? | Yes |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|------------------------------------------------------|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 15 February 2008 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 15 February 2008 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Immunogenicity:

-To assess the seroprotection rates (Diphtheria, Tetanus, polio types 1, 2 and 3, and Polyrribosyl Ribitol Phosphate conjugated to Tetanus protein [PRP]) and seroconversion rates (Pertussis toxoid, Filamentous Hemagglutinin [FHA]) of Sanofi Pasteur's DTacP-IPV//PRP~T combined vaccine, one month after the three-dose primary vaccination.

-To describe the immunogenicity of the study combined vaccine (PENTAXIM™) one month after the three-dose primary vaccination (Visit 5), prior to the booster dose (at Visit 6) and one month after the booster dose (Visit 7).

-To describe the immunogenicity of the recombinant hepatitis B vaccine antigen one month after the three-dose primary vaccination (Visit 5) and approximately 14 to 15 months later (Visit 6).

Safety:

-To describe the safety after each dose of the study combined vaccine (PENTAXIM™).

-To describe the safety after each dose of recombinant hepatitis B vaccine.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were 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. Appropriate medical equipment was also available on site in case of any immediate allergic reactions.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

| | |
|-----------------------------------------------------------|-----------------|
| Actual start date of recruitment | 18 October 2005 |
| 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 | South Africa: 212 |
| Worldwide total number of subjects | 212 |
| 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) | 212 |
| 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:

Study subjects were enrolled from 18 October 2005 to 01 July 2006 at 1 clinic center in South Africa.

Pre-assignment

Screening details:

A total of 212 subjects who met all inclusion and none of the exclusion criteria were enrolled and vaccinated in the study.

Period 1

| | |
|------------------------------|----------------|
| Period 1 title | Primary Phase |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Blinding implementation details:

Not applicable

Arms

| | |
|-----------|-------------|
| Arm title | Study group |
|-----------|-------------|

Arm description:

Subjects received DTacP-IPV//PRP-T vaccine (PENTAXIM™) at 6, 10, and 14 weeks of age and hepatitis B vaccine (HEBERBIOVAC®) at 6, 10, and 14 weeks of age.

| | |
|----------------------------------------|-----------------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL, intramuscular into the right anterolateral external aspect of the upper thigh, 1 injection each at 6, 10, and 14 weeks of age.

| | |
|----------------------------------------|---------------------------------------|
| Investigational medicinal product name | Hepatitis B vaccine (HEBERBIOVAC HB®) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL, intramuscular into the left anterolateral external aspect of the upper thigh, 1 injection each at 6, 10, and 14 weeks of age.

| Number of subjects in period 1 | Study group |
|--------------------------------|-------------|
| Started | 212 |
| Completed | 207 |
| Not completed | 5 |
| Serious adverse events | 1 |
| Lost to follow-up | 1 |

| | |
|--------------------|---|
| Protocol deviation | 3 |
|--------------------|---|

Period 2

| | |
|----------------------------------|----------------|
| Period 2 title | Booster Phase |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |
| Blinding implementation details: | |
| Not applicable | |

Arms

| | |
|-----------------------------------------------------------------------------------------|-----------------------------------------------|
| Arm title | Study group |
| Arm description: | |
| Subjects received a booster dose of DTacP-IPV//PRP~T vaccine at 18 to 19 months of age. | |
| Arm type | Experimental |
| Investigational medicinal product name | DTacP-IPV//PRP~T combined vaccine (PENTAXIM™) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL, intramuscular into the right anterolateral external aspect of the upper thigh, 1 injection each at 6, 10, and 14 weeks of age.

| Number of subjects in period 2 | Study group |
|--------------------------------------------------|-------------|
| Started | 207 |
| Completed | 179 |
| Not completed | 29 |
| Consent withdrawn by subject | 9 |
| Serious adverse events | 2 |
| Lost to follow-up | 15 |
| Protocol deviation | 3 |
| Joined | 1 |
| Withdrawn from study and re-included for booster | 1 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------|
| Reporting group title | Study group |
| Reporting group description: Subjects received DTacP-IPV//PRP-T vaccine (PENTAXIM™) at 6, 10, and 14 weeks of age and hepatitis B vaccine (HEBERBIOVAC®) at 6, 10, and 14 weeks of age. | |

| Reporting group values | Study group | Total | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------|-------|--|
| Number of subjects | 212 | 212 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 212 | 212 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 0 | 0 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| The Study group and Immunogenicity Analysis Set age is reported in days (standard deviation) whereas the Immunogenicity Analysis Set Pre-Booster and Immunogenicity Analysis Set Post-Booster age is reported in months (standard deviation). | | | |
| Units: days | | | |
| arithmetic mean | 43.2 | | |
| standard deviation | ± 1.6 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 105 | 105 | |
| Male | 107 | 107 | |

Subject analysis sets

| | |
|----------------------------|-----------------------------------------|
| Subject analysis set title | Immunogenicity Analysis Set Post-dose 3 |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

The Immunogenicity Analysis Set was defined as all infants who received DTacP-IPV//PRP~T at Visit 02 (Day 42), Visit 03 (Day 70), and Visit 04 (Day 98) without any delays, had a blood sample performed at Visit 05 (Day 126; blood sample 02) without any delays, and had an antibody titration available in blood sample 02.

| | |
|----------------------------|-----------------------------------------|
| Subject analysis set title | Immunogenicity Analysis Set Pre-Booster |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Immunogenicity Analysis Set Pre-Booster was defined as all subjects who had received the DTacP-IPV//PRP-T combined vaccine on Visit 02 (Day 42), Visit 03 (Day 70), and Visit 04 (Day 98), had a blood sample performed on Visit 06 (Visit 05 + 14-15 months; blood sample 03), age at blood sample on Visit 06 (blood sample 03) less than 17 months (no older than 20 months), and had an antibody titer available for blood sample 03.

| | |
|----------------------------|------------------------------------------|
| Subject analysis set title | Immunogenicity Analysis Set Post-Booster |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Immunogenicity Analysis Set Post-Booster was defined as all subjects who received the vaccination with DTacP-IPV//PRP~T combined vaccine on Visit 02 (Day 42), Visit 03 (Day 70), Visit 04 (Day 98) or Visit 06 (Visit 05 + 14-15 months) who were < 17 months (no older than 20 months) on Visit 06, had a blood sample performed on Visit 07 (Visit 06 + 28-42 days) without any delays, and had an antibody titer available for blood sample 04.

| Reporting group values | Immunogenicity Analysis Set Post-dose 3 | Immunogenicity Analysis Set Pre-Booster | Immunogenicity Analysis Set Post-Booster |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|-----------------------------------------|------------------------------------------|
| Number of subjects | 206 | 180 | 176 |
| 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) | 206 | 180 | 176 |
| 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 | | | |
| The Study group and Immunogenicity Analysis Set age is reported in days (standard deviation) whereas the Immunogenicity Analysis Set Pre-Booster and Immunogenicity Analysis Set Post-Booster age is reported in months (standard deviation). | | | |
| Units: days | | | |
| arithmetic mean | 43.2 | 18.3 | 18.3 |
| standard deviation | ± 1.6 | ± 0.4 | ± 0.4 |
| Gender categorical Units: Subjects | | | |
| Female | 99 | 86 | 83 |
| Male | 107 | 94 | 93 |

End points

End points reporting groups

| | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|
| Reporting group title | Study group |
| Reporting group description: Subjects received DTacP-IPV//PRP-T vaccine (PENTAXIM™) at 6, 10, and 14 weeks of age and hepatitis B vaccine (HEBERBIOVAC®) at 6, 10, and 14 weeks of age. | |
| Reporting group title | Study group |
| Reporting group description: Subjects received a booster dose of DTacP-IPV//PRP~T vaccine at 18 to 19 months of age. | |
| Subject analysis set title | Immunogenicity Analysis Set Post-dose 3 |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: The Immunogenicity Analysis Set was defined as all infants who received DTacP-IPV//PRP~T at Visit 02 (Day 42), Visit 03 (Day 70), and Visit 04 (Day 98) without any delays, had a blood sample performed at Visit 05 (Day 126; blood sample 02) without any delays, and had an antibody titration available in blood sample 02. | |
| Subject analysis set title | Immunogenicity Analysis Set Pre-Booster |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Immunogenicity Analysis Set Pre-Booster was defined as all subjects who had received the DTacP-IPV//PRP-T combined vaccine on Visit 02 (Day 42), Visit 03 (Day 70), and Visit 04 (Day 98), had a blood sample performed on Visit 06 (Visit 05 + 14-15 months; blood sample 03), age at blood sample on Visit 06 (blood sample 03) less than 17 months (no older than 20 months), and had an antibody titer available for blood sample 03. | |
| Subject analysis set title | Immunogenicity Analysis Set Post-Booster |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Immunogenicity Analysis Set Post-Booster was defined as all subjects who received the vaccination with DTacP-IPV//PRP~T combined vaccine on Visit 02 (Day 42), Visit 03 (Day 70), Visit 04 (Day 98) or Visit 06 (Visit 05 + 14-15 months) who were < 17 months (no older than 20 months) on Visit 06, had a blood sample performed on Visit 07 (Visit 06 + 28-42 days) without any delays, and had an antibody titer available for blood sample 04. | |

Primary: Percentage of Subjects with Seroconversion/Seroconversion to Vaccine Antigens One Month After A Three Dose Primary Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) Concomitantly with Hepatitis B Vaccine (HEBERBIOVAC™)

| | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Subjects with Seroconversion/Seroconversion to Vaccine Antigens One Month After A Three Dose Primary Vaccination with DTacP-IPV// PRP~T Combined Vaccine (PENTAXIM™) Concomitantly with Hepatitis B Vaccine (HEBERBIOVAC™) ^[1] |
| End point description: Anti-Diphtheria, Anti-Tetanus, Anti-Pertussis toxoid, Anti-Filamentous hemagglutinin (FHA) were assessed by enzyme-linked immunosorbent assay (ELISA). Anti-Polio types 1, 2, and 3 were assessed by seroneutralization. Anti-Polyribosyl Ribitol Phosphate conjugated to Tetanus protein (PRP) was assessed by Farr type radioimmunoassay and Anti-Hepatitis B surface antigen were assessed by radioimmunoassay. Seroconversion for Anti-Diphtheria and Anti-Tetanus was defined as antibody titers ≥ 0.1 IU/mL, ≥ 8 (dil) for Anti-Polio types 1, 2, and 3, ≥ 0.15 µg/mL for Anti-PRP, and ≥ 10 mIU/mL for Hepatitis B. Seroconversion for Anti-Pertussis toxoid and Anti-FHA was defined as antibody titers ≥ 2-fold and ≥ 4-fold increase EU/mL. | |
| End point type | Primary |
| End point timeframe: 1 month post-dose 3 of primary 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 study group and the study vaccine administered for this outcome.

| End point values | Study group | | | |
|------------------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 206 | | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Anti-Diphtheria | 100 | | | |
| Anti-Tetanus | 100 | | | |
| Anti-Polio 1 | 100 | | | |
| Anti-Polio 2 | 100 | | | |
| Anti-Polio 3 | 100 | | | |
| Anti-PRP | 94.6 | | | |
| Anti-Pertussis toxoid; ≥ 2 -fold increase | 99 | | | |
| Anti-Pertussis toxoid; ≥ 4 -fold increase | 97.5 | | | |
| Anti-FHA; ≥ 2 -fold increase | 94.6 | | | |
| Anti-FHA; ≥ 4 -fold increase | 83.9 | | | |
| Anti-Hepatitis B | 100 | | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Titers of Antibodies Against Vaccine Antigens One Month After A Three Dose Primary Vaccination with DTacP-IPV// PRP~T Combined Vaccine (PENTAXIM™) Concomitantly with Hepatitis B Vaccine (HEBERBIOVAC™)

| | |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Geometric Mean Titers of Antibodies Against Vaccine Antigens One Month After A Three Dose Primary Vaccination with DTacP-IPV// PRP~T Combined Vaccine (PENTAXIM™) Concomitantly with Hepatitis B Vaccine (HEBERBIOVAC™) |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Anti-Diphtheria was assessed by ELISA and seroneutralization. Anti-Tetanus, Anti-Pertussis toxoid, Anti-Filamentous hemagglutinin (FHA) were assessed by enzyme-linked immunosorbent assay (ELISA). Anti-Polio types 1, 2, and 3 were assessed by seroneutralization. Anti-Polyribosyl Ribitol Phosphate conjugated to Tetanus protein (PRP) was assessed by Farr type radioimmunoassay and Anti-Hepatitis B surface antigen were assessed by radioimmunoassay.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

1 month post-dose 3 of primary vaccination

| | | | | |
|------------------------------------------|-----------------------------------------|--|--|--|
| End point values | Immunogenicity Analysis Set Post-dose 3 | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 206 | | | |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-Diphtheria (ELISA) | 0.9 (0.82 to 0.99) | | | |
| Anti-Diphtheria (seroneutralization) | 0.05 (0.04 to 0.06) | | | |
| Anti-Tetanus | 0.78 (0.71 to 0.85) | | | |
| Anti-Pertussis toxoid | 382.61 (353.13 to 414.55) | | | |
| Anti-FHA | 161 (145.94 to 177.61) | | | |
| Anti-Polio 1 | 1453.05 (1235.9 to 1708.35) | | | |
| Anti-Polio 2 | 1699.14 (1410.88 to 2046.29) | | | |
| Anti-Polio 3 | 2398.17 (1979.8 to 2904.96) | | | |
| Anti-PRP | 1.97 (1.55 to 2.51) | | | |
| Anti-Hepatitis B | 929.21 (786.39 to 1097.97) | | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects with Seroprotection/Seroconversion to Vaccine Antigens Post-Booster Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) After a Primary Series with DTacP-IPV//PRP~T Vaccine Concomitantly with Hepatitis B (HEBERBIOVAC™)

| | |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Subjects with Seroprotection/Seroconversion to Vaccine Antigens Post-Booster Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) After a Primary Series with DTacP-IPV//PRP~T Vaccine Concomitantly with Hepatitis B (HEBERBIOVAC™) |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Anti-Diphtheria was assessed by ELISA and seroneutralization. Anti-Tetanus, Anti-Pertussis toxoid, Anti-Filamentous hemagglutinin (FHA) were assessed by enzyme-linked immunosorbent assay (ELISA). Anti-Polio types 1, 2, and 3 were assessed by seroneutralization. Anti-Polyribosyl Ribitol Phosphate conjugated to Tetanus protein (PRP) was assessed by Farr type radioimmunoassay and Anti-Hepatitis B surface antigen were assessed by radioimmunoassay. Seroprotection for Anti-Diphtheria and Anti-Tetanus was defined as antibody titers ≥ 0.1 IU/mL, ≥ 8 (dil) for Anti-Polio types 1, 2, and 3, ≥ 0.15 μ g/mL for Anti-PRP, and ≥ 10 mIU/mL for Hepatitis B. Seroconversion for Anti-Pertussis toxoid and Anti-FHA was defined as antibody titers ≥ 2 -fold and ≥ 4 -fold increase EU/mL.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:
Post-booster vaccination

| End point values | Immunogenicity Analysis Set Post-Booster | | | |
|-----------------------------------------------|------------------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 176 | | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Anti-Diphtheria (ELISA) | 100 | | | |
| Anti-Diphtheria (Seroneutralization) | 100 | | | |
| Anti-Tetanus | 100 | | | |
| Anti-Polio 1 | 100 | | | |
| Anti-Polio 2 | 100 | | | |
| Anti-Polio 3 | 100 | | | |
| Anti-PRP | 100 | | | |
| Anti-Pertussis toxoid; \geq 2-fold increase | 100 | | | |
| Anti-Pertussis toxoid; \geq 4-fold increase | 98.4 | | | |
| Anti-FHA; \geq 2-fold increase | 98.6 | | | |
| Anti-FHA; \geq 4-fold increase | 95.7 | | | |
| Anti-Hepatitis (Pre-booster) | 99.4 | | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Titers of Antibodies Against Vaccine Antigens Post-Booster Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) After a Primary Series with DTacP-IPV//PRP~T Combined Vaccine Concomitantly with Hepatitis B Vaccine (HEBERBIOVAC™)

| | |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Geometric Mean Titers of Antibodies Against Vaccine Antigens Post-Booster Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) After a Primary Series with DTacP-IPV//PRP~T Combined Vaccine Concomitantly with Hepatitis B Vaccine (HEBERBIOVAC™) |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Anti-Diphtheria, Anti-Tetanus, Anti-Pertussis toxoid, Anti-Filamentous hemagglutinin (FHA) were assessed by enzyme-linked immunosorbent assay (ELISA). Anti-Polio types 1, 2, and 3 were assessed by seroneutralization. Anti-Polyribosyl Ribitol Phosphate conjugated to Tetanus protein (PRP) was assessed by Farr type radioimmunoassay.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

1 month post-booster vaccination

| End point values | Immunogenicity Analysis Set Post-dose 3 | Immunogenicity Analysis Set Pre-Booster | Immunogenicity Analysis Set Post-Booster | |
|------------------------------------------|-----------------------------------------|-----------------------------------------|------------------------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 176 | 175 | 176 | |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-Diphtheria | 0.9 (0.82 to 1) | 0.04 (0.03 to 0.05) | 3.72 (3.18 to 4.35) | |
| Anti-Tetanus | 0.79 (0.72 to 0.86) | 0.17 (0.15 to 0.2) | 9.23 (8.1 to 10.51) | |
| Anti-Pertussis toxoid | 390.62 (359.03 to 424.97) | 11.21 (9.64 to 13.05) | 465.51 (419.47 to 516.61) | |
| Anti-FHA | 160.18 (143.55 to 178.74) | 12.89 (10.41 to 15.96) | 520.35 (465.28 to 581.95) | |
| Anti-Polio 1 | 1459.62 (1219.02 to 1747.7) | 233.85 (166.86 to 327.73) | 8928.86 (7639.93 to 10435.25) | |
| Anti-Polio 2 | 1634.12 (1343.97 to 1986.91) | 302.95 (217.92 to 421.16) | 6608.29 (5633.61 to 7751.59) | |
| Anti-Polio 3 | 2328.15 (1882.84 to 2878.77) | 360.1 (254.69 to 509.15) | 12119.89 (10247.37 to 14334.58) | |
| Anti-PRP | 2.26 (1.79 to 2.86) | 0.35 (0.26 to 0.46) | 47.01 (37.7 to 58.62) | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Titer Ratios of Antibodies Against Vaccine Antigens Post-Booster Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) After a Primary Series with DTacP-IPV//PRP~T Combined Vaccine Concomitantly with Hepatitis B (HEBERBIOVAC™)

| | |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Geometric Mean Titer Ratios of Antibodies Against Vaccine Antigens Post-Booster Vaccination with DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM™) After a Primary Series with DTacP-IPV//PRP~T Combined Vaccine Concomitantly with Hepatitis B (HEBERBIOVAC™) |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Anti-Diphtheria, Anti-Tetanus, Anti-Pertussis toxoid, Anti-Filamentous hemagglutinin (FHA) were assessed by enzyme-linked immunosorbent assay (ELISA). Anti-Polio types 1, 2, and 3 were assessed by seroneutralization. Anti-Polyribosyl Ribitol Phosphate conjugated to Tetanus protein (PRP) was assessed by Farr type radioimmunoassay.

Geometric mean titer ratios are only reported for Anti-Pertussis toxoid and Anti-FHA for the Immunogenicity Analysis Set Post-dose 3.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Visit 06 (Visit 05 + 14-15 months, where Visit 05 is Day 126) and Visit 07 (Visit 06 + 28-42 days)

| End point values | Immunogenicity Analysis Set Post-dose 3 | Immunogenicity Analysis Set Post-Booster | | |
|------------------------------------------|-----------------------------------------|------------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 175 | 175 | | |
| Units: Titer ratios (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-Diphtheria | 0 (0 to 0) | 101.1 (85.58 to 119.45) | | |
| Anti-Tetanus | 0 (0 to 0) | 56.16 (47.92 to 65.8) | | |
| Anti-Pertussis toxoid | 53 (42.65 to 65.85) | 39.4 (33.18 to 46.77) | | |
| Anti-FHA | 16.17 (13.04 to 20.04) | 40.74 (33.88 to 48.98) | | |
| Anti-Polio 1 | 0 (0 to 0) | 35.34 (24.13 to 51.78) | | |
| Anti-Polio 2 | 0 (0 to 0) | 22.24 (15.25 to 32.42) | | |
| Anti-Polio 3 | 0 (0 to 0) | 33.07 (22.27 to 49.12) | | |
| Anti-PRP | 0 (0 to 0) | 134.12 (100.66 to 178.7) | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following Any Primary Vaccination with DTacP-IPV// PRP~T Combined Vaccine (PENTAXIM™) Concomitantly with Hepatitis B Vaccine (HEBERBIOVAC™)

| | |
|------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following Any Primary Vaccination with DTacP-IPV// PRP~T Combined Vaccine (PENTAXIM™) Concomitantly with Hepatitis B Vaccine (HEBERBIOVAC™) |
| End point description: | Solicited injection site reactions: Tenderness, Erythema, and Swelling. Solicited systemic reactions: Fever, Vomiting, Crying abnormal, Drowsiness, Appetite lost, and Irritability. |
| End point type | Other pre-specified |
| End point timeframe: | |
| Post-any primary vaccination | |

| End point values | Study group | | | |
|-------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 212 | | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Injection site Tenderness | 70.3 | | | |
| Injection site Erythema | 47.2 | | | |

| | | | | |
|-------------------------|------|--|--|--|
| Injection site Swelling | 45.3 | | | |
| Fever | 35.8 | | | |
| Vomiting | 42.9 | | | |
| Crying abnormal | 64.6 | | | |
| Drowsiness | 48.1 | | | |
| Appetite lost | 35.8 | | | |
| Irritability | 55.7 | | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following Any Primary Vaccination with DTacP-IPV// PRP~T Combined Vaccine (PENTAXIM™) Concomitantly with Hepatitis B Vaccine (HEBERBIOVAC™)

| | |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following Any Primary Vaccination with DTacP-IPV// PRP~T Combined Vaccine (PENTAXIM™) Concomitantly with Hepatitis B Vaccine (HEBERBIOVAC™) |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Solicited injection site reactions: Tenderness, Erythema, and Swelling. Solicited systemic reactions: Fever, Vomiting, Crying abnormal, Drowsiness, Appetite lost, and Irritability.

Grade 3 solicited injection site reactions: Tenderness, Cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling, ≥ 5 cm. Grade 3 systemic reactions: Fever, $\geq 39.0^{\circ}\text{C}$; Vomiting, ≥ 6 episodes per 24 hours or requiring parenteral hydration; Crying abnormal, > 3 hours; Drowsiness, Sleeping most of the time or difficult to wake up; Appetite lost, Refuses ≥ 3 feeds or refuses most feeds; Irritability, Inconsolable.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Day 0 up to Day 8 post-any and each vaccination and per injected dose

| End point values | Study group | | | |
|-----------------------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 212 | | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Any Inj. site Tenderness; Post-Any; PENTAXIM | 68.4 | | | |
| Grade 3 Inj. site Tenderness; Post-Any; PENTAXIM | 0 | | | |
| Any Inj. site Tenderness; Post-Any; HEBERBIOVAC | 65.6 | | | |
| Grade 3 Inj. site Tenderness; Post-Any; HEBERBIOVAC | 0 | | | |
| Any Inj. site Tenderness; Post-dose 1; PENTAXIM | 54 | | | |
| Grade 3 Inj. site Tenderness; Post-dose 1; PENTAXIM | 0 | | | |
| Any Inj. site Tenderness; Post-dose 1; HEBERBIOVAC | 49.3 | | | |

| | | | | |
|------------------------------------------------------|------|--|--|--|
| Gr 3 Inj. site Tenderness; Post-dose 1; HEBERBIOVAC | 0.5 | | | |
| Any Inj. site Tenderness; Post-dose 2; PENTAXIM | 49 | | | |
| Grade 3 Inj. site Tenderness; Post-dose 2; PENTAXIM | 1.4 | | | |
| Any Inj. site Tenderness; Post-dose 2; HEBERBIOVAC | 44.8 | | | |
| Gr 3 Inj. site Tenderness; Post-dose 2; HEBERBIOVAC | 1.4 | | | |
| Any Inj. site Tenderness; Post-dose 3; PENTAXIM | 41.5 | | | |
| Grade 3 Inj. site Tenderness; Post-dose 3; PENTAXIM | 0.5 | | | |
| Any Inj. site Tenderness; Post-dose 3; HEBERBIOVAC | 36.7 | | | |
| Gr 3 Inj. site Tenderness; Post-dose 3; HEBERBIOVAC | 0 | | | |
| Any Inj. site Erythema; Post-Any; PENTAXIM | 45.3 | | | |
| Grade 3 Inj. site Erythema; Post-Any; PENTAXIM | 0 | | | |
| Any Inj. site Erythema; Post-Any; HEBERBIOVAC | 36.8 | | | |
| Grade 3 Inj. site Erythema; Post-Any; HEBERBIOVAC | 0 | | | |
| Any Inj. site Erythema; Post-dose 1; PENTAXIM | 30.3 | | | |
| Grade 3 Inj. site Erythema; Post-dose 1; PENTAXIM | 0 | | | |
| Any Inj. site Erythema; Post-dose 1; HEBERBIOVAC | 25.6 | | | |
| Grade 3 Inj. site Erythema; Post-dose 1; HEBERBIOVAC | 0 | | | |
| Any Inj. site Erythema; Post-dose 2; PENTAXIM | 26.2 | | | |
| Grade 3 Inj. site Erythema; Post-dose 2; PENTAXIM | 0 | | | |
| Any Inj. site Erythema; Post-dose 2; HEBERBIOVAC | 20 | | | |
| Grade 3 Inj. site Erythema; Post-dose 2; HEBERBIOVAC | 0 | | | |
| Any Inj. site Erythema; Post-dose 3; PENTAXIM | 26.1 | | | |
| Grade 3 Inj. site Erythema; Post-dose 3; PENTAXIM | 0 | | | |
| Any Inj. site Erythema; Post-dose 3; HEBERBIOVAC | 18.8 | | | |
| Grade 3 Inj. site Erythema; Post-dose 3; HEBERBIOVAC | 0 | | | |
| Any Inj. site Swelling; Post-Any; PENTAXIM | 42 | | | |
| Grade 3 Inj. site Swelling; Post-Any; PENTAXIM | 0 | | | |
| Any Inj. site Swelling; Post-Any; HEBERBIOVAC | 37.7 | | | |
| Grade 3 Inj. site Swelling; Post-Any; HEBERBIOVAC | 0 | | | |
| Any Inj. site Swelling; Post-dose 1; PENTAXIM | 23.7 | | | |
| Grade 3 Inj. site Swelling; Post-dose 1; PENTAXIM | 0 | | | |

| | | | | |
|------------------------------------------------------|------|--|--|--|
| Any Inj. site Swelling; Post-dose 1; HEBERBIOVAC | 20.4 | | | |
| Grade 3 Inj. site Swelling; Post-dose 1; HEBERBIOVAC | 0 | | | |
| Any Inj. site Swelling; Post-dose 2; PENTAXIM | 25.2 | | | |
| Grade 3 Inj. site Swelling; Post-dose 2; PENTAXIM | 0 | | | |
| Any Inj. site Swelling; Post-dose 2; HEBERBIOVAC | 19 | | | |
| Grade 3 Inj. site Swelling; Post-dose 2; HEBERBIOVAC | 0 | | | |
| Any Inj. site Swelling; Post-dose 3; PENTAXIM | 28.5 | | | |
| Grade 3 Inj. site Swelling; Post-dose 3; PENTAXIM | 0 | | | |
| Any Inj. site Swelling; Post-dose 3; HEBERBIOVAC | 23.7 | | | |
| Grade 3 Inj. site Swelling; Post-dose 3; HEBERBIOVAC | 0 | | | |
| Any Fever; Post-Any injection | 35.8 | | | |
| Grade 3 Fever; Post-Any injection | 0 | | | |
| Any Fever; Post-dose 1 | 17.6 | | | |
| Grade 3 Fever; Post-dose 1 | 1.4 | | | |
| Any Fever; Post-dose 2 | 12.4 | | | |
| Grade 3 Fever; Post-dose 2 | 0.5 | | | |
| Any Fever; Post-dose 3 | 14 | | | |
| Grade 3 Fever; Post-dose 3 | 0 | | | |
| Any Vomiting; Post-Any injection | 42.9 | | | |
| Grade 3 Vomiting; Post-Any injection | 0 | | | |
| Any Vomiting; Post-dose 1 | 29.4 | | | |
| Grade 3 Vomiting; Post-dose 1 | 0.5 | | | |
| Any Vomiting; Post-dose 2 | 18.1 | | | |
| Grade 3 Vomiting; Post-dose 2 | 0.5 | | | |
| Any Vomiting; Post-dose 3 | 17.9 | | | |
| Grade 3 Vomiting; Post-dose 3 | 0.5 | | | |
| Any Crying abnormal; Post-Any injection | 64.6 | | | |
| Grade 3 Crying abnormal; Post-Any injection | 0 | | | |
| Any Crying abnormal; Post-dose 1 | 48.3 | | | |
| Grade 3 Crying abnormal; Post-dose 1 | 1.4 | | | |
| Any Crying abnormal; Post-dose 2 | 36.7 | | | |
| Grade 3 Crying abnormal; Post-dose 2 | 1.4 | | | |
| Any Crying abnormal; Post-dose 3 | 29 | | | |
| Grade 3 Crying abnormal; Post-dose 3 | 1 | | | |
| Any Drowsiness; Post-Any injection | 48.1 | | | |
| Grade 3 Drowsiness; Post-Any injection | 0 | | | |
| Any Drowsiness; Post-dose 1 | 33.2 | | | |
| Grade 3 Drowsiness; Post-dose 1 | 0.5 | | | |
| Any Drowsiness; Post-dose 2 | 25.2 | | | |
| Grade 3 Drowsiness; Post-dose 2 | 0.5 | | | |
| Any Drowsiness; Post-dose 3 | 18.4 | | | |
| Grade 3 Drowsiness; Post-dose 3 | 0.5 | | | |
| Any Appetite lost; Post-Any injection | 35.8 | | | |
| Grade 3 Appetite lost; Post-Any injection | 0 | | | |

| | | | | |
|------------------------------------------|------|--|--|--|
| Any Appetite lost; Post-dose 1 | 20.9 | | | |
| Grade 3 Appetite lost; Post-dose 1 | 0.5 | | | |
| Any Appetite lost; Post-dose 2 | 17.1 | | | |
| Grade 3 Appetite lost; Post-dose 2 | 0.5 | | | |
| Any Appetite lost; Post-dose 3 | 19.3 | | | |
| Grade 3 Appetite lost; Post-dose 3 | 1 | | | |
| Any Irritability; Post-Any injection | 55.7 | | | |
| Grade 3 Irritability; Post-Any injection | 0 | | | |
| Any Irritability; Post-dose 1 | 46 | | | |
| Grade 3 Irritability; Post-dose 1 | 0.5 | | | |
| Any Irritability; Post-dose 2 | 30.5 | | | |
| Grade 3 Irritability; Post-dose 2 | 1 | | | |
| Any Irritability; Post-dose 3 | 26.1 | | | |
| Grade 3 Irritability; Post-dose 3 | 1.4 | | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects with Solicited Injection-site and Systemic Reactions After A Booster with DTacP-IPV//PRP~T Vaccine (PENTAXIM) After a Primary Series with DTacP-IPV//PRP~T Vaccine (PENTAXIM) Concomitantly with Hepatitis B (HEBERBIOVAC)

| | |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Subjects with Solicited Injection-site and Systemic Reactions After A Booster with DTacP-IPV//PRP~T Vaccine (PENTAXIM) After a Primary Series with DTacP-IPV//PRP~T Vaccine (PENTAXIM) Concomitantly with Hepatitis B (HEBERBIOVAC) |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Solicited injection site reactions: Tenderness, Erythema, and Swelling. Solicited systemic reactions: Fever, Vomiting, Crying abnormal, Drowsiness, Appetite lost, and Irritability.

Grade 3 solicited injection site reactions: Tenderness, Cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling, ≥ 5 cm. Grade 3 systemic reactions: Fever, $\geq 39.0^{\circ}\text{C}$; Vomiting, ≥ 6 episodes per 24 hours or requiring parenteral hydration; Crying abnormal, > 3 hours; Drowsiness, Sleeping most of the time or difficult to wake up; Appetite lost, Refuses ≥ 3 feeds or refuses most feeds; Irritability, Inconsolable.

| | |
|--------------------------|---------------------|
| End point type | Other pre-specified |
| End point timeframe: | |
| Post-booster vaccination | |

| End point values | Study group | | | |
|-----------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 180 | | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Any Injection site Tenderness | 60.6 | | | |
| Grade 3 Injection site Tenderness | 7.2 | | | |
| Any Injection site Erythema | 39.4 | | | |

| | | | | |
|---------------------------------|------|--|--|--|
| Grade 3 Injection site Erythema | 3.3 | | | |
| Any Injection site Swelling | 39.4 | | | |
| Grade 3 Injection site Swelling | 3.9 | | | |
| Any Fever | 29.4 | | | |
| Grade 3 Fever | 1.7 | | | |
| Any Vomiting | 11.7 | | | |
| Grade 3 Vomiting | 1.1 | | | |
| Any Crying abnormal | 36.1 | | | |
| Grade 3 Crying abnormal | 1.7 | | | |
| Any Drowsiness | 26.1 | | | |
| Grade 3 Drowsiness | 1.1 | | | |
| Any Appetite lost | 32.8 | | | |
| Grade 3 Appetite lost | 3.3 | | | |
| Any Irritability | 31.7 | | | |
| Grade 3 Irritability | 1.1 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from Day 0 post-vaccination up to 1 month post-booster vaccination.

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

Dictionary used

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

| | |
|--------------------|---|
| Dictionary version | 9 |
|--------------------|---|

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | Study group |
|-----------------------|-------------|

Reporting group description:

Subjects received DTacP-IPV//PRP-T vaccine (PENTAXIM™) at 6, 10, and 14 weeks of age and hepatitis B vaccine (HEBERBIOVAC®) at 6, 10, and 14 weeks of age.

| Serious adverse events | Study group | | |
|---------------------------------------------------|-------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 25 / 212 (11.79%) | | |
| number of deaths (all causes) | 2 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Dehydration with acidosis herbal intoxication | | | |
| subjects affected / exposed | 1 / 212 (0.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Epilepsy | | | |
| subjects affected / exposed | 1 / 212 (0.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Gastrooesophageal reflux | | | |
| subjects affected / exposed | 1 / 212 (0.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Gastroenteritis | | | |

| | | | | |
|-------------------------------------------------|-----------------|--|--|--|
| subjects affected / exposed | 6 / 212 (2.83%) | | | |
| occurrences causally related to treatment / all | 0 / 7 | | | |
| deaths causally related to treatment / all | 0 / 2 | | | |
| Bronchopneumonia | | | | |
| subjects affected / exposed | 7 / 212 (3.30%) | | | |
| occurrences causally related to treatment / all | 0 / 7 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Viral bronchiolitis | | | | |
| subjects affected / exposed | 1 / 212 (0.47%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchiolitis | | | | |
| subjects affected / exposed | 7 / 212 (3.30%) | | | |
| occurrences causally related to treatment / all | 0 / 10 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia | | | | |
| subjects affected / exposed | 3 / 212 (1.42%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Acute gastroenteritis | | | | |
| subjects affected / exposed | 1 / 212 (0.47%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bilateral bronchopneumonia | | | | |
| subjects affected / exposed | 1 / 212 (0.47%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Streptococcus viridans septicemia | | | | |
| subjects affected / exposed | 1 / 212 (0.47%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary tuberculosis | | | | |

| | | | |
|-------------------------------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 212 (0.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Study group | | |
|-------------------------------------------------------|--------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 145 / 212 (68.40%) | | |
| Nervous system disorders | | | |
| Drowsiness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 102 / 212 (48.11%) | | |
| occurrences (all) | 102 | | |
| General disorders and administration site conditions | | | |
| Injection site Tenderness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 145 / 212 (68.40%) | | |
| occurrences (all) | 145 | | |
| Injection site Erythema | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 96 / 212 (45.28%) | | |
| occurrences (all) | 96 | | |
| Injection site Swelling | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 89 / 212 (41.98%) | | |
| occurrences (all) | 89 | | |
| Fever | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 76 / 212 (35.85%) | | |
| occurrences (all) | 76 | | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 14 / 212 (6.60%) | | |
| occurrences (all) | 14 | | |

| | | | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|--|--|
| Vomiting alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 91 / 212 (42.92%) 91 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) | 21 / 212 (9.91%) 21 13 / 212 (6.13%) 13 | | |
| Skin and subcutaneous tissue disorders Dermatitis subjects affected / exposed occurrences (all) | 15 / 212 (7.08%) 15 | | |
| Psychiatric disorders Crying abnormal alternative assessment type: Systematic subjects affected / exposed occurrences (all) Irritability alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 137 / 212 (64.62%) 137 118 / 212 (55.66%) 118 | | |
| Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all) Rhinitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) | 19 / 212 (8.96%) 19 27 / 212 (12.74%) 27 81 / 212 (38.21%) 81 | | |
| Metabolism and nutrition disorders | | | |

| | | | |
|--------------------------------------------|-------------------|--|--|
| Appetite lost | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 76 / 212 (35.85%) | | |
| occurrences (all) | 76 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|----------------------------------------------------------------------|
| 05 January 2006 | Informed investigators of the protocol to replace screening failures |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported