



Clinical trial results:

A pivotal open label, two-arm, multi-center trial to evaluate the safety and immunogenicity of a single dose of Adacel® vaccine in persons 10 to <11 years of age with the intent to extend the licensure of Adacel vaccine for use in children 10 years of age.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2015-005627-84 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 28 June 2011 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 20 April 2016 |
| First version publication date | 20 April 2016 |

Trial information

Trial identification

| | |
|-----------------------|-------|
| Sponsor protocol code | Td519 |
|-----------------------|-------|

Additional study identifiers

| | |
|------------------------------------|-----------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01311557 |
| WHO universal trial number (UTN) | U1111-1115-6619 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Sanofi Pasteur Inc. |
| Sponsor organisation address | 1 Discovery Drive, Swiftwater, United States, 18370 |
| Public contact | Medical Team Leader, Sanofi Pasteur Inc., 1 570-957-3289, david.greenberg@sanofipasteur.com |
| Scientific contact | Medical Team Leader, Sanofi Pasteur Inc., 1 570-957-3289, david.greenberg@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? | 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 | 28 September 2012 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 28 June 2011 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

1) To compare pertussis antibody responses induced by Adacel in persons 10 to <11 years of age to those induced by Adacel in persons 11 to <12 years of age.

2) To compare the booster responses against pertussis antigens induced by Adacel in persons 10 to <11 years of age to those induced by Adacel in persons 11 to <12 years 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. 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 | 07 March 2011 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | United States: 1302 |
| Worldwide total number of subjects | 1302 |
| EEA total number of subjects | 0 |

Notes:

Subjects enrolled per age group

| | |
|---|------|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 1302 |

| | |
|---------------------------|---|
| 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 07 March 2011 to 19 May 2011 at 36 clinical centers in the United States.

Pre-assignment

Screening details:

A total of 1302 subjects who met all inclusion criteria and none of the exclusion criteria were enrolled and vaccinated.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall trial (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 | Subjects 10 to <11 Years of Age |
|------------------|---------------------------------|

Arm description:

Subjects received 1 dose of Adacel® vaccine at Visit 1.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Adacel®) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL, intramuscular, 1 injection on Day 0 (Visit 1).

| | |
|------------------|---------------------------------|
| Arm title | Subjects 11 to <12 Years of Age |
|------------------|---------------------------------|

Arm description:

Subjects received 1 dose of Adacel® vaccine at Visit 1.

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Adacel®) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL, intramuscular, 1 injection on Day 0 (Visit 1).

| Number of subjects in period 1 | Subjects 10 to <11 Years of Age | Subjects 11 to <12 Years of Age |
|---------------------------------------|------------------------------------|------------------------------------|
| Started | 651 | 651 |
| Completed | 646 | 645 |
| Not completed | 5 | 6 |
| Consent withdrawn by subject | 1 | 2 |
| Serious adverse event | - | 1 |
| Lost to follow-up | - | 1 |
| Protocol deviation | 4 | 2 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------------------------|
| Reporting group title | Subjects 10 to <11 Years of Age |
|-----------------------|---------------------------------|

Reporting group description:

Subjects received 1 dose of Adacel® vaccine at Visit 1.

| | |
|-----------------------|---------------------------------|
| Reporting group title | Subjects 11 to <12 Years of Age |
|-----------------------|---------------------------------|

Reporting group description:

Subjects received 1 dose of Adacel® vaccine at Visit 1.

| Reporting group values | Subjects 10 to <11 Years of Age | Subjects 11 to <12 Years of Age | Total |
|---|------------------------------------|------------------------------------|-------|
| Number of subjects | 651 | 651 | 1302 |
| 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) | 0 | 0 | 0 |
| Children (2-11 years) | 651 | 651 | 1302 |
| 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: years | | | |
| arithmetic mean | 10.5 | 11.4 | |
| standard deviation | ± 0.3 | ± 0.3 | - |
| Gender categorical Units: Subjects | | | |
| Female | 305 | 315 | 620 |
| Male | 346 | 336 | 682 |

End points

End points reporting groups

| | |
|---|---------------------------------|
| Reporting group title | Subjects 10 to <11 Years of Age |
| Reporting group description: Subjects received 1 dose of Adacel® vaccine at Visit 1. | |
| Reporting group title | Subjects 11 to <12 Years of Age |
| Reporting group description: Subjects received 1 dose of Adacel® vaccine at Visit 1. | |

Primary: Summary of Geometric Mean Titers of Anti-Pertussis Titers Following a Single Dose of Adacel® Vaccine

| | |
|--|--|
| End point title | Summary of Geometric Mean Titers of Anti-Pertussis Titers Following a Single Dose of Adacel® Vaccine |
| End point description: Anti-Pertussis titers (Pertussis toxoid [PT], Filamentous hemagglutinin [FHA], Pertactin [PRN], Fimbriae types 2 and 3 [FIM] geometric mean titers were assessed by enzyme-linked immunosorbent assay (ELISA). | |
| End point type | Primary |
| End point timeframe: Day 30 post-vaccination | |

| End point values | Subjects 10 to <11 Years of Age | Subjects 11 to <12 Years of Age | | |
|--|---------------------------------|---------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 613 | 608 | | |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-Pertussis toxoid | 30.1 (28 to 32.4) | 32 (29.6 to 34.7) | | |
| Anti-Filamentous hemagglutinin | 232 (218 to 247) | 225 (211 to 239) | | |
| Anti-Pertactin | 464 (426 to 506) | 444 (408 to 482) | | |
| Anti-Fimbriae types 2 and 3 | 477 (413 to 550) | 540 (478 to 611) | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Non-inferiority (PT; GMT Ratio) |
| Statistical analysis description: Non-inferiority comparison of post-vaccination anti-Pertussis geometric mean titers between groups. | |
| Comparison groups | Subjects 10 to <11 Years of Age v Subjects 11 to <12 Years of Age |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 1221 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[1] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.94 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.843 |
| upper limit | 1.05 |

Notes:

[1] - A two-sided 95% confidence interval (CI) was constructed around each of the ratios: Pertussis toxoid (PT) GMT Group 1/GMT Group 2. The GMT hypothesis was supported by the data if the lower bound of the calculated 95% CI was > 0.67. This was the equivalent of testing the null hypothesis using a one-sided type I error rate of 0.025. The post-vaccination anti-PT GMTs in Adacel recipients in Group 1 were non-inferior to the post-vaccination GMTs in Adacel recipients in Group 2.

| | |
|-----------------------------------|----------------------------------|
| Statistical analysis title | Non-inferiority (FHA; GMT Ratio) |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Non-inferiority comparison of post-vaccination anti-Filamentous hemagglutinin geometric mean titers between groups.

| | |
|---|---|
| Comparison groups | Subjects 10 to <11 Years of Age v Subjects 11 to <12 Years of Age |
| Number of subjects included in analysis | 1221 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[2] |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.03 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.944 |
| upper limit | 1.13 |

Notes:

[2] - A two-sided 95% confidence interval (CI) was constructed around each of the ratios: Filamentous hemagglutinin (FHA) GMT Group 1/GMT Group 2. The GMT hypothesis was supported by the data if the lower bound of the calculated 95% CI was > 0.67. This was the equivalent of testing the null hypothesis using a one-sided type I error rate of 0.025. The post-vaccination anti-FHA GMTs in Adacel recipients in Group 1 were non-inferior to the post-vaccination GMTs in Adacel recipients in Group 2.

| | |
|-----------------------------------|----------------------------------|
| Statistical analysis title | Non-inferiority (PRN; GMT Ratio) |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Non-inferiority comparison of post-vaccination anti-Pertactin geometric mean titers between groups.

| | |
|---|---|
| Comparison groups | Subjects 10 to <11 Years of Age v Subjects 11 to <12 Years of Age |
| Number of subjects included in analysis | 1221 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[3] |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.05 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.928 |
| upper limit | 1.18 |

Notes:

[3] - A two-sided 95% confidence interval (CI) was constructed around each of the ratios: Pertactin (PRN) GMT Group 1/GMT Group 2. The GMT hypothesis was supported by the data if the lower bound of the calculated 95% CI was > 0.67. This was the equivalent of testing the null hypothesis using a one-sided type I error rate of 0.025. The post-vaccination anti-PRN GMTs in Adacel recipients in Group 1 were non-inferior to the post-vaccination GMTs in Adacel recipients in Group 2.

| | |
|--|---|
| Statistical analysis title | Non-inferiority (FIM; GMT Ratio) |
| Statistical analysis description: | |
| Non-inferiority comparison of post-vaccination anti-Fimbriae types 2 and 3 geometric mean titers between groups. | |
| Comparison groups | Subjects 10 to <11 Years of Age v Subjects 11 to <12 Years of Age |
| Number of subjects included in analysis | 1221 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[4] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.882 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.731 |
| upper limit | 1.06 |

Notes:

[4] - A two-sided 95% confidence interval (CI) was constructed around each of the ratios: Fimbriae types 2 and 3 (FIM) GMT Group 1/GMT Group 2. The GMT hypothesis was supported by the data if the lower bound of the calculated 95% CI was > 0.67. This was the equivalent of testing the null hypothesis using a one-sided type I error rate of 0.025. The post-vaccination anti-FIM GMTs in Adacel recipients in Group 1 were non-inferior to the post-vaccination GMTs in Adacel recipients in Group 2.

Primary: Summary of Anti-Pertussis Booster Response Following a Booster Dose of Adacel® Vaccine

| | |
|-----------------|---|
| End point title | Summary of Anti-Pertussis Booster Response Following a Booster Dose of Adacel® Vaccine ^[5] |
|-----------------|---|

End point description:

Anti-Pertussis booster responses were assessed by enzyme-linked immunosorbent assay (ELISA). For pertussis antigens (Pertussis toxoid [PT], filamentous hemagglutinin [FHA], pertactin [PRN], fimbriae types 2 and 3 [FIM], a booster response rate was defined as a four-fold increase in pre- to post-vaccination titers for subjects with pre-vaccination titers ≤ 93 ELISA Unit (EU)/mL for PT, ≤ 170 EU/mL for FHA, ≤ 115 EU/mL for PRN, and ≤ 285 EU/mL for FIM. If the pre-vaccination titers were > 93 EU/mL for PT, > 170 EU/mL for FHA, > 115 EU/mL for PRN, or > 285 EU/mL for FIM then a two-fold increase in the antibody titer was defined as a booster response.

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

End point timeframe:

30 days post-vaccination

Notes:

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

Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

| End point values | Subjects 10 to <11 Years of Age | Subjects 11 to <12 Years of Age | | |
|-------------------------------|---------------------------------|---------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 613 | 608 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Anti-Pertussis toxoid | 56.7 | 56.1 | | |

| | | | | |
|--------------------------------|------|------|--|--|
| Anti-Filamentous hemagglutinin | 84.2 | 84.8 | | |
| Anti-Pertactin | 98 | 97.5 | | |
| Anti-Fimbriae types 2 and 3 | 93.7 | 97.1 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Summary of Anti-Tetanus and Anti-Diphtheria Booster Response Following a Booster Dose of Adacel® Vaccine

| | |
|-----------------|---|
| End point title | Summary of Anti-Tetanus and Anti-Diphtheria Booster Response Following a Booster Dose of Adacel® Vaccine ^[6] |
|-----------------|---|

End point description:

Anti-Tetanus booster responses were assessed by enzyme-linked immunosorbent assay (ELISA). Anti-Diphtheria booster responses were assessed by a toxin neutralization test. Booster response rate was defined as a four-fold increase in pre- to post-vaccination titers for subjects with pre-vaccination titers \leq 2.56 EU/mL for diphtheria and \leq 2.7 EU/mL for tetanus. If the pre-vaccination titers were $>$ 2.56 EU/mL for diphtheria or $>$ 2.7 EU/mL for tetanus, then a two-fold increase in response rate was defined as a booster response.

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

End point timeframe:

30 days post-vaccination

Notes:

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

Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

| End point values | Subjects 10 to <11 Years of Age | Subjects 11 to <12 Years of Age | | |
|-------------------------------|---------------------------------|---------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 613 | 608 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Anti-Tetanus | 98.5 | 98.8 | | |
| Anti-Diphtheria | 97.7 | 98 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Seroprotection To Tetanus and Diphtheria Following a Single Dose of Adacel® Vaccine

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Seroprotection To Tetanus and Diphtheria Following a Single Dose of Adacel® Vaccine |
|-----------------|---|

End point description:

Anti-tetanus seroprotection rates were assessed by enzyme-linked immunosorbent assay (ELISA). Anti-diphtheria seroprotection was assessed by toxin neutralization test. Seroprotection was defined as post-vaccination antibody titers \geq 0.1 IU/mL.

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

End point timeframe:

Day 0 (pre-vaccination) and 30 days post-vaccination

| End point values | Subjects 10 to <11 Years of Age | Subjects 11 to <12 Years of Age | | |
|------------------------------------|---------------------------------|---------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 613 | 608 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Anti-Tetanus (Pre-vaccination) | 90.3 | 91.2 | | |
| Anti-Tetanus (Post-vaccination) | 99.7 | 100 | | |
| Anti-Diphtheria (Pre-vaccination) | 83.6 | 75.9 | | |
| Anti-Diphtheria (Post-vaccination) | 99.7 | 100 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Anti-Pertussis Geometric Mean Titers Before and Post-vaccination With a Single Dose of Adacel® Vaccine

| | |
|-----------------|---|
| End point title | Summary of Anti-Pertussis Geometric Mean Titers Before and Post-vaccination With a Single Dose of Adacel® Vaccine |
|-----------------|---|

End point description:

Anti-Pertussis titers (Pertussis toxoid [PT], Filamentous hemagglutinin [FHA], Pertactin [PRN], Fimbriae types 2 and 3 [FIM]) geometric mean titers were assessed by enzyme-linked immunosorbent assay (ELISA).

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

End point timeframe:

Day 0 (pre-vaccination) and Day 30 post-vaccination

| End point values | Subjects 10 to <11 Years of Age | Subjects 11 to <12 Years of Age | | |
|--|---------------------------------|---------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 613 | 608 | | |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-Pertussis toxoid; Day 0 | 4.96 (4.54 to 5.42) | 4.85 (4.41 to 5.34) | | |
| Anti-Pertussis toxoid; Day 30 | 30.1 (28 to 32.4) | 32 (29.6 to 34.7) | | |
| Anti-Filamentous hemagglutinin; Day 0 | 22.1 (20.1 to 24.2) | 20.3 (18.5 to 22.3) | | |
| Anti-Filamentous hemagglutinin; Day 30 | 232 (218 to 247) | 225 (211 to 239) | | |

| | | | | |
|-------------------------------------|---------------------|---------------------|--|--|
| Anti-Pertactin; Day 0 | 15.6 (14.2 to 17.1) | 14.8 (13.5 to 16.2) | | |
| Anti-Pertactin; Day 30 | 464 (426 to 506) | 444 (408 to 482) | | |
| Anti-Fimbriae types 2 and 3; Day 0 | 6.77 (6.05 to 7.57) | 7.07 (6.33 to 7.89) | | |
| Anti-Fimbriae types 2 and 3; Day 30 | 477 (413 to 550) | 540 (478 to 611) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Reporting Solicited Injection-site and Systemic Reactions Following A Single Dose of Adacel® Vaccine

| | |
|-----------------|---|
| End point title | Percentage of Subjects Reporting Solicited Injection-site and Systemic Reactions Following A Single Dose of Adacel® Vaccine |
|-----------------|---|

End point description:

Solicited injection-site: Pain, Erythema and Swelling. Solicited systemic reactions: Fever, Headache, Malaise, and Myalgia.

Grade 3 Solicited Injection-site reactions: Pain, Incapacitating, unable to perform usual activities; Erythema and Swelling, ≥ 50 mm. Grade 3 Solicited systemic reactions: Fever, $\geq 39.0^{\circ}\text{C}$ or $\geq 102.1^{\circ}\text{F}$; Headache, Malaise, and Myalgia, Significant, prevents daily activity.

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

End point timeframe:

Day 0 up to Day 7 post-vaccination

| End point values | Subjects 10 to <11 Years of Age | Subjects 11 to <12 Years of Age | | |
|---------------------------------|---------------------------------|---------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 650 | 649 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Injection-site Pain | 80.9 | 80.9 | | |
| Grade 3 Injection-site Pain | 3.3 | 2.2 | | |
| Injection-site Erythema | 39.4 | 38.4 | | |
| Grade 3 Injection-site Erythema | 7.9 | 7.4 | | |
| Injection-site Swelling | 35.2 | 33.5 | | |
| Grade 3 Injection-site Swelling | 8.4 | 7.3 | | |
| Fever | 1.6 | 0.6 | | |
| Grade 3 Fever | 0 | 0.2 | | |
| Headache | 33.1 | 37.6 | | |
| Grade 3 Headache | 2 | 1.9 | | |
| Malaise | 26.2 | 29.3 | | |
| Grade 3 Malaise | 1.9 | 2.8 | | |
| Myalgia | 49.1 | 56.4 | | |
| Grade 3 Myalgia | 3.3 | 1.7 | | |

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 up to Day 30 post-vaccination.

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

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 13 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|---------------------------------|
| Reporting group title | Subjects 10 to <11 Years of Age |
|-----------------------|---------------------------------|

Reporting group description:

Subjects received 1 dose of Adacel® vaccine on Day 0 (Visit 1).

| | |
|-----------------------|---------------------------------|
| Reporting group title | Subjects 11 to <12 Years of Age |
|-----------------------|---------------------------------|

Reporting group description:

Subjects received 1 dose of Adacel® vaccine on Day 0 (Visit 1).

| Serious adverse events | Subjects 10 to <11 Years of Age | Subjects 11 to <12 Years of Age | |
|---|------------------------------------|------------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 650 (0.00%) | 1 / 649 (0.15%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 650 (0.00%) | 1 / 649 (0.15%) | |
| 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 | Subjects 10 to <11 Years of Age | Subjects 11 to <12 Years of Age | |
|---|------------------------------------|------------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 521 / 650 (80.15%) | 522 / 649 (80.43%) | |
| Nervous system disorders | | | |
| Headache | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 213 / 650 (32.77%) | 243 / 649 (37.44%) | |
| occurrences (all) | 213 | 243 | |

| | | | |
|--|--------------------|--------------------|--|
| General disorders and administration site conditions | | | |
| Injection-site Erythema | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 254 / 650 (39.08%) | 248 / 649 (38.21%) | |
| occurrences (all) | 254 | 248 | |
| Injection-site Pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 521 / 650 (80.15%) | 522 / 649 (80.43%) | |
| occurrences (all) | 521 | 522 | |
| Injection-site Swelling | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 227 / 650 (34.92%) | 216 / 649 (33.28%) | |
| occurrences (all) | 227 | 216 | |
| Malaise | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 169 / 650 (26.00%) | 189 / 649 (29.12%) | |
| occurrences (all) | 169 | 189 | |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 316 / 650 (48.62%) | 364 / 649 (56.09%) | |
| occurrences (all) | 316 | 364 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 10 February 2011 | The planned trial period was revised; booster responses (tetanus and diphtheria) were updated as primary objectives; non-inferiority analysis of booster response rates was added as a primary endpoint; booster response rates (tetanus and diphtheria) were updated to primary endpoints; primary hypothesis was revised; planned sample size and schedule of procedures were amended to include a time window for post-vaccination and recording of safety data, respectively; exclusion criteria were modified; and statistical and assessment methods were revised. |
| 11 March 2011 | Exclusion criterion was modified to improve clarity. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported