



Clinical trial results:

Comparison of the immunogenicity and safety of a combined adsorbed low dose diphtheria, tetanus and inactivated poliomyelitis vaccine (REVAXIS®) with a combined diphtheria, tetanus and inactivated poliomyelitis vaccine (DT Polio®) when given as a booster dose at 6 years of age.

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2005-001446-16 |
| Trial protocol | FR |
| Global end of trial date | 16 January 2008 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 27 April 2016 |
| First version publication date | 29 May 2015 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | F05-TdI-301 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00447525 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Sanofi Pasteur MSD S.N.C. |
| Sponsor organisation address | 162 avenue Jean Jaurès - CS 50712, Lyon Cedex 07, France, 69367 |
| Public contact | Clinical Trials Disclosure, Sanofi Pasteur MSD S.N.C, ClinicalTrialsDisclosure@spmsd.com |
| Scientific contact | Clinical Trials Disclosure, Sanofi Pasteur MSD S.N.C, ClinicalTrialsDisclosure@spmsd.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 | 16 January 2008 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 January 2008 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the Diphtheria seroprotection response (defined as anti-diphtheria antibody titre (SN) ≥ 0.1 IU/mL), the Tetanus seroprotection response (defined as an anti-tetanus antibody titre (EIA) ≥ 0.1 IU/mL), and the Poliomyelitis type 1, 2 & 3 seroprotection responses (defined as an anti-poliovirus antibody type 1, 2 & 3 titre (SN) ≥ 8 (1/dil)) 1 month (28 to 35 days) after a single dose of REVAXIS® (dT-IPV vaccine) is non inferior to the Diphtheria, Tetanus and Poliomyelitis type 1, 2 & 3 seroprotection responses 1 month after a single dose of DT Polio® (DT-IPV vaccine) when given as a second booster to healthy 6 year-old children who received 3-dose primary series within the first 6 months of life and a first booster at 16-18 months of life (+/-2 months) including DT-IPV vaccine.

Protection of trial subjects:

Subjects in the study received a single dose of the study vaccine or comparator vaccine supplied in a pre-filled 0.5 mL syringe that was administered by qualified study personnel.
Subjects with allergy to any of the vaccine components were not vaccinated.
After each vaccination, subjects were also kept under observation for 20 minutes to ensure their safety.
Appropriate equipment were also available on site in case of any immediate allergic reactions.

Background therapy:

Children were previously vaccinated with 3 doses of a diphtheria, tetanus and poliomyelitis containing vaccine given alone or in combination within the first 6 months of life and a booster dose of a diphtheria, tetanus and poliomyelitis containing vaccine given alone or in combination at 16-18 months of life (+/-2 months).

Evidence for comparator:

The comparator group (DT Polio Group) was added in order to answer the study objective.
Indeed, this study was designed to provide comparative data of the immunogenicity and the safety of REVAXIS versus DT Polio when given as a booster dose at 6 years of age.
DT Polio was a reference vaccine licensed and recommended as diphtheria, tetanus and poliovirus booster at 6 years of age in France.

| | |
|---|-----------------|
| Actual start date of recruitment | 24 January 2007 |
| 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 | France: 760 |
| Worldwide total number of subjects | 760 |
| EEA total number of subjects | 760 |

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) | 760 |
| 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 participants were recruited for the study between 24 January 2007 and 10 December 2007 in 71 active centres in France.

Pre-assignment

Screening details:

788 subjects were screened in this study.

760 subjects were randomised.

759 subjects met all inclusion criteria and none of the non-inclusion criteria.

758 subjects were vaccinated and completed the study.

Period 1

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

Blinding implementation details:

Blinding is not applicable as this study was an open-label study.

Arms

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

Arm description:

Participants received a single dose of REVAXIS (diphtheria, tetanus and poliomyelitis (inactivated) vaccine (adsorbed, reduced antigen(s) content)).

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | REVAXIS® |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

One 0.5 mL dose (intramuscular, deltoid) at 6 years of age.

| | |
|------------------|----------------|
| Arm title | DT Polio Group |
|------------------|----------------|

Arm description:

Participants received a single dose of DT Polio (diphtheria, tetanus and inactivated poliovirus vaccine).

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | DT Polio® |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

One 0.5 mL dose (intramuscular, deltoid) at 6 years of age.

| Number of subjects in period 1 | REVAXIS Group | DT Polio Group |
|---------------------------------------|---------------|----------------|
| Started | 384 | 376 |
| Vaccinated | 383 | 375 |
| Completed | 383 | 375 |
| Not completed | 1 | 1 |
| Consent withdrawn by subject | - | 1 |
| Protocol deviation | 1 | - |

Baseline characteristics

Reporting groups

| | |
|--|----------------|
| Reporting group title | REVAXIS Group |
| Reporting group description: | |
| Participants received a single dose of REVAXIS (diphtheria, tetanus and poliomyelitis (inactivated) vaccine (adsorbed, reduced antigen(s) content)). | |
| Reporting group title | DT Polio Group |
| Reporting group description: | |
| Participants received a single dose of DT Polio (diphtheria, tetanus and inactivated poliovirus vaccine). | |

| Reporting group values | REVAXIS Group | DT Polio Group | Total |
|--|---------------|----------------|-------|
| Number of subjects | 384 | 376 | 760 |
| Age categorical | | | |
| Units: Subjects | | | |
| Children (2-11 years) | 384 | 376 | 760 |
| Age continuous | | | |
| Age in years at vaccination (1 missing value in the REVAXIS group) | | | |
| Units: years | | | |
| arithmetic mean | 6.4 | 6.4 | |
| standard deviation | ± 0.3 | ± 0.3 | - |
| Gender categorical | | | |
| Female and male | | | |
| Units: Subjects | | | |
| Female | 182 | 180 | 362 |
| Male | 202 | 196 | 398 |
| Weight continuous | | | |
| Weight in kg at vaccination | | | |
| Units: kg | | | |
| arithmetic mean | 22.4 | 22.6 | |
| standard deviation | ± 3.6 | ± 3.8 | - |
| Height continuous | | | |
| Height in cm at vaccination | | | |
| Units: cm | | | |
| arithmetic mean | 119 | 119.2 | |
| standard deviation | ± 5.3 | ± 5.5 | - |

End points

End points reporting groups

| | |
|--|----------------|
| Reporting group title | REVAXIS Group |
| Reporting group description: | |
| Participants received a single dose of REVAXIS (diphtheria, tetanus and poliomyelitis (inactivated) vaccine (adsorbed, reduced antigen(s) content)). | |
| Reporting group title | DT Polio Group |
| Reporting group description: | |
| Participants received a single dose of DT Polio (diphtheria, tetanus and inactivated poliovirus vaccine). | |

Primary: Seroprotection against diphtheria (SN), tetanus (EIA), and polio 1, 2 & 3 (SN) one month after one dose of REVAXIS vaccine or DT Polio vaccine

| | |
|--|--|
| End point title | Seroprotection against diphtheria (SN), tetanus (EIA), and polio 1, 2 & 3 (SN) one month after one dose of REVAXIS vaccine or DT Polio vaccine |
| End point description: | |
| On day 0 (D0), study participants were blood sampled and then received 1 dose of study or comparator vaccine. One month later (i.e., 28 to 35 days post vaccination), study participants were blood sampled. Antibody titres were measured using seroneutralisation method (SN) for diphtheria and polio 1, 2 & 3, enzyme immunoassay (EIA) for diphtheria and tetanus. Seroprotection was defined as a titre ≥ 0.10 IU/mL for diphtheria (SN), ≥ 0.10 IU/mL for tetanus (EIA), ≥ 8 (1/dil) for polio 1, 2 & 3 (SN). Analysis was done on the Per Protocol set. | |
| Note: (N=***, ***) represents the number of assessed subjects in the REVAXIS and DT Polio groups, respectively. | |
| End point type | Primary |
| End point timeframe: | |
| One month (28 to 35 days) after vaccination. | |

| End point values | REVAXIS Group | DT Polio Group | | |
|---|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 284 | 283 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Anti-Diphtheria ≥ 0.10 IU/mL (SN) (N=284, 283) | 98.6 (96.4 to 99.6) | 99.3 (97.5 to 99.9) | | |
| Anti-Tetanus ≥ 0.10 IU/mL (EIA) (N=284, 283) | 99.6 (98.1 to 100) | 100 (98.7 to 100) | | |
| Anti-Polio 1 ≥ 8 (1/dil) (SN) (N=284, 283) | 100 (98.7 to 100) | 100 (98.7 to 100) | | |
| Anti-Polio 2 ≥ 8 (1/dil) (SN) (N=284, 283) | 100 (98.7 to 100) | 100 (98.7 to 100) | | |
| Anti-Polio 3 ≥ 8 (1/dil) (SN) (N=284, 282) | 100 (98.7 to 100) | 100 (98.7 to 100) | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Non-inferiority analysis for diphtheria (SN) |
| Statistical analysis description: | |
| The estimate of the difference between groups in the diphtheria, tetanus and poliomyelitis type 1, 2 & 3 seroprotection rates was calculated with their two-sided 95% confidence interval (CI). If all lower bounds of the 95% CIs of the difference were higher than -5 % (i.e the non-inferiority margin) it was concluded that the REVAXIS Group was non-inferior to the DT Polio Group. Analysis was done on the Per Protocol set. | |
| Comparison groups | REVAXIS Group v DT Polio Group |
| Number of subjects included in analysis | 567 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[1] |
| Method | Wilson score method without CC |
| Parameter estimate | Difference in percentages of subjects |
| Point estimate | -0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.9 |
| upper limit | 1.3 |

Notes:

[1] - The immune response of REVAXIS vaccine was considered as non-inferior to DT Polio vaccine if the lower bound of the 2-sided 95% CI of the difference in the percentages of subjects with antibody titres ≥ 0.10 IU/mL for diphtheria (SN) was greater than -5%.

CI was based on the Wilson score method without continuity correction (CC).

| | |
|--|--|
| Statistical analysis title | Non inferiority analysis for tetanus (EIA) |
| Statistical analysis description: | |
| The estimate of the difference between groups in the diphtheria, tetanus and poliomyelitis type 1, 2 & 3 seroprotection rates was calculated with their two-sided 95% confidence interval (CI). If all lower bounds of the 95% CIs of the difference were higher than -5 % (i.e the non-inferiority margin) it was concluded that the REVAXIS Group was non-inferior to the DT Polio Group. Analysis was done on the Per Protocol set. | |
| Comparison groups | REVAXIS Group v DT Polio Group |
| Number of subjects included in analysis | 567 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[2] |
| Method | Wilson score method without CC |
| Parameter estimate | Difference in percentages of subjects |
| Point estimate | -0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2 |
| upper limit | 1 |

Notes:

[2] - The immune response of REVAXIS vaccine was considered as non-inferior to DT Polio vaccine if the lower bound of the 2-sided 95% CI of the difference in the percentages of subjects with antibody titres ≥ 0.10 IU/mL for tetanus (EIA) was greater than -5%.

CI was based on the Wilson score method without continuity correction (CC).

| | |
|--|---|
| Statistical analysis title | Non inferiority analysis for Polio 1 (SN) |
| Statistical analysis description: | |
| The estimate of the difference between groups in the diphtheria, tetanus and poliomyelitis type 1, 2 & 3 seroprotection rates was calculated with their two-sided 95% confidence interval (CI). If all lower bounds of the 95% CIs of the difference were higher than -5 % (i.e the non-inferiority margin) it was | |

concluded that the REVAXIS Group was non-inferior to the DT Polio Group.
Analysis was done on the Per Protocol set.

| | |
|---|---------------------------------------|
| Comparison groups | REVAXIS Group v DT Polio Group |
| Number of subjects included in analysis | 567 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[3] |
| Method | Wilson score method without CC |
| Parameter estimate | Difference in percentages of subjects |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 1.3 |

Notes:

[3] - The immune response of REVAXIS vaccine was considered as non-inferior to DT Polio vaccine if the lower bound of the 2-sided 95% CI of the difference in the percentages of subjects with antibody titres ≥ 8 (1/dil for polio 1 (SN) was greater than -5%.

CI was based on the Wilson score method without continuity correction (CC).

| | |
|-----------------------------------|---|
| Statistical analysis title | Non inferiority analysis for Polio 2 (SN) |
|-----------------------------------|---|

Statistical analysis description:

The estimate of the difference between groups in the diphtheria, tetanus and poliomyelitis type 1, 2 & 3 seroprotection rates was calculated with their two-sided 95% confidence interval (CI). If all lower bounds of the 95% CIs of the difference were higher than -5 % (i.e the non-inferiority margin) it was concluded that the REVAXIS Group was non-inferior to the DT Polio Group.

Analysis was done on the Per Protocol set.

| | |
|---|---------------------------------------|
| Comparison groups | REVAXIS Group v DT Polio Group |
| Number of subjects included in analysis | 567 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[4] |
| Method | Wilson score method without CC |
| Parameter estimate | Difference in percentages of subjects |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 1.3 |

Notes:

[4] - The immune response of REVAXIS vaccine was considered as non-inferior to DT Polio vaccine if the lower bound of the 2-sided 95% CI of the difference in the percentages of subjects with antibody titres ≥ 8 (1/dil) for polio 2 (SN) was greater than -5%.

CI was based on the Wilson score method without continuity correction (CC).

| | |
|-----------------------------------|---|
| Statistical analysis title | Non inferiority analysis for Polio 3 (SN) |
|-----------------------------------|---|

Statistical analysis description:

The estimate of the difference between groups in the diphtheria, tetanus and poliomyelitis type 1, 2 & 3 seroprotection rates was calculated with their two-sided 95% confidence interval (CI). If all lower bounds of the 95% CIs of the difference were higher than -5 % (i.e the non-inferiority margin) it was concluded that the REVAXIS Group was non-inferior to the DT Polio Group.

Analysis was done on the Per Protocol set.

| | |
|-------------------|--------------------------------|
| Comparison groups | REVAXIS Group v DT Polio Group |
|-------------------|--------------------------------|

| | |
|---|---------------------------------------|
| Number of subjects included in analysis | 567 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[5] |
| Method | Wilson score method without CC |
| Parameter estimate | Difference in percentages of subjects |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 1.3 |

Notes:

[5] - The immune response of REVAXIS vaccine was considered as non-inferior to DT Polio vaccine if the lower bound of the 2-sided 95% CI of the difference in the percentages of subjects with antibody titres ≥ 8 (1/dil) for polio 3 (SN) was greater than -5%.

CI was based on the Wilson score method without continuity correction (CC).

Secondary: Geometric Mean Titres of anti-diphtheria, anti-tetanus and anti-polio 1, 2 & 3 antibodies one month after one dose of REVAXIS vaccine or DT Polio vaccine

| | |
|-----------------|---|
| End point title | Geometric Mean Titres of anti-diphtheria, anti-tetanus and anti-polio 1, 2 & 3 antibodies one month after one dose of REVAXIS vaccine or DT Polio vaccine |
|-----------------|---|

End point description:

On day 0 (D0), study participants were blood sampled and then received 1 dose of study or comparator vaccine. One month later (28 to 35 days, i.e., post vaccination), study participants were blood sampled. Antibody titres were measured using seroneutralisation method (SN) for diphtheria and polio 1, 2 & 3, enzyme immunoassay (EIA) for diphtheria and tetanus. Antibody titres are expressed in IU/mL for diphtheria (SN), for diphtheria (EIA), and for tetanus (EIA), and 1/dil for polio 1, 2 & 3 (SN).

Analysis was done on the Per Protocol set.

Note: (N=***, ***) represents the number of assessed subjects in the REVAXIS and DT Polio groups, respectively.

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

End point timeframe:

One month (28 to 35 days) after vaccination.

| End point values | REVAXIS Group | DT Polio Group | | |
|--|------------------------------|------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 284 | 283 | | |
| Units: Titres | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-Diphtheria (SN) (N=284, 283) | 3.71 (3.14 to 4.38) | 23.32 (19.52 to 27.85) | | |
| Anti-Diphtheria (EIA) (N=284, 281) | 1.9 (1.65 to 2.19) | 8.31 (7.24 to 9.54) | | |
| Anti-Tetanus (EIA) (N=284, 283) | 9.38 (8.33 to 10.56) | 13.87 (12.21 to 15.76) | | |
| Anti-Polio 1 (SN) (N=284, 283) | 4776.77 (4093.41 to 5574.21) | 7705.41 (6681.88 to 8885.73) | | |
| Anti-Polio 2 (SN) (N=284, 283) | 5715.35 (4919.35 to 6640.16) | 4534.24 (3931.99 to 5228.73) | | |

| | | | | |
|--------------------------------|------------------------------------|-----------------------------------|--|--|
| Anti-Polio 3 (SN) (N=284, 282) | 6015.97 (5138.41 to 7043.41) | 2248.5 (1906.62 to 2651.69) | | |
|--------------------------------|------------------------------------|-----------------------------------|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Response rates for diphtheria (SN & EIA) and tetanus (EIA) one month after one dose of REVAXIS vaccine or DT Polio vaccine

| | |
|-----------------|--|
| End point title | Response rates for diphtheria (SN & EIA) and tetanus (EIA) one month after one dose of REVAXIS vaccine or DT Polio vaccine |
|-----------------|--|

End point description:

On day 0 (D0), study participants were blood sampled and then received 1 dose of study or comparator vaccine. One month later (28 to 35 days, i.e., post vaccination), study participants were blood sampled. Antibody titres were measured using seroneutralisation method (SN) for diphtheria and polio 1, 2 & 3, enzyme immunoassay (EIA) for diphtheria and tetanus.

Thresholds were defined as titres ≥ 1.0 IU/mL for diphtheria (SN), ≥ 0.10 IU/mL and ≥ 1.0 IU/mL for diphtheria (EIA), ≥ 1.0 IU/mL for tetanus (EIA).

Analysis was done on the Per Protocol set.

Note: (N=***, ***) represents the number of assessed subjects in the REVAXIS and DT Polio groups, respectively.

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

End point timeframe:

One month (28 to 35 days) after vaccination.

| End point values | REVAXIS Group | DT Polio Group | | |
|---|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 284 | 283 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Anti-Diphtheria ≥ 1.0 IU/mL (SN) (N=284, 283) | 85.9 (81.3 to 89.7) | 98.6 (96.4 to 99.6) | | |
| Anti-Diphtheria ≥ 0.1 IU/mL (EIA) (N=284, 281) | 98.6 (96.4 to 99.6) | 99.6 (98 to 100) | | |
| Anti-Diphtheria ≥ 1.0 IU/mL (EIA) (N=284, 281) | 71.1 (65.5 to 76.3) | 95 (91.8 to 97.2) | | |
| Anti-Tetanus ≥ 1.0 IU/mL (EIA) (N=284, 283) | 98.6 (96.4 to 99.6) | 97.5 (95 to 99) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean of (individual) Titres Ratios of anti-diphtheria, anti-tetanus and anti-polio 1, 2 & 3 antibodies one month after one dose of REVAXIS vaccine or DT Polio vaccine

| | |
|--|--|
| End point title | Geometric Mean of (individual) Titres Ratios of anti-diphtheria, anti-tetanus and anti-polio 1, 2 & 3 antibodies one month after one dose of REVAXIS vaccine or DT Polio vaccine |
| End point description: On day 0 (D0), study participants were blood sampled and then received 1 dose of study or comparator vaccine. One month later (28 to 35 days, i.e., post vaccination), study participants were blood sampled. Antibody titres were measured using seroneutralisation method (SN) for diphtheria and polio 1, 2 & 3, enzyme immunoassay (EIA) for diphtheria and tetanus. Individual post (D28) / pre (D0) antibody titre ratios were measured for diphtheria, tetanus and polio 1, 2 & 3. Analysis was done on the Per Protocol set. | |
| Note: (N=***, ***) represents the number of assessed subjects in the REVAXIS and DT Polio groups, respectively. | |
| End point type | Secondary |
| End point timeframe: One month (28 to 35 days) after vaccination. | |

| End point values | REVAXIS Group | DT Polio Group | | |
|--|------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 284 | 283 | | |
| Units: Not applicable | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-Diphtheria (SN) (N=284, 283) | 58.62 (47.59 to 72.2) | 307.62 (247.53 to 382.31) | | |
| Anti-Diphtheria (EIA) (N=284, 280) | 27.79 (23.75 to 32.52) | 112.23 (97.28 to 129.47) | | |
| Anti-Tetanus (EIA) (N=284, 283) | 38.7 (33.37 to 44.89) | 58.95 (51.61 to 67.32) | | |
| Anti-Polio 1 (SN) (N=283, 282) | 63.52 (49.07 to 82.23) | 121.98 (93.58 to 159.02) | | |
| Anti-Polio 2 (SN) (N=284, 283) | 56.92 (44.28 to 73.17) | 54.11 (42 to 69.71) | | |
| Anti-Polio 3 (SN) (N=284, 282) | 51.51 (40.26 to 65.89) | 23.68 (18.88 to 29.68) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of safety (D0-D28)

| | |
|--|----------------------------|
| End point title | Summary of safety (D0-D28) |
| End point description: Adverse events (AEs) were reported onto the diary card by the parent(s) or legal representative: - From day 0 (D0) to D7 for solicited injection-site adverse reactions (ISRs: injection site pain, erythema, and swelling) and solicited systemic AEs (headache, myalgia, pyrexia); - From D0 to Visit 2 for unsolicited (spontaneously reported) ISRs and systemic AEs. AEs at injection sites were always considered as related to vaccine (Injection-Site Reactions (ISRs)). The investigator had to assess whether systemic AEs were related or not to the vaccine. All (related and unrelated) are displayed here. Descriptive analysis was done on the Safety Analysis set. | |

One subject was randomised in the DT Polio Group but received REVAXIS vaccine. The subject was thus included in the REVAXIS Group in the Safety Analysis set, which therefore included 384 subjects in the REVAXIS group, and 374 subjects in the DT Polio Group.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| One month (28 to 35 days) after vaccination. | |

| End point values | REVAXIS Group | DT Polio Group | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 384 | 374 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| D0 to D28, any AE | 83.1 | 85.6 | | |
| D0 to D7, any AE | 82.6 | 84.2 | | |
| D0 to D7, ISR | 76 | 78.6 | | |
| D0 to D7, solicited ISR | 76 | 78.6 | | |
| D0 to D7, unsolicited ISR | 3.4 | 5.6 | | |
| D0 to D7, systemic AE | 42.4 | 40.9 | | |
| D0 to D7, solicited systemic AE | 35.4 | 36.4 | | |
| D0 to D7, unsolicited systemic AE | 12.2 | 12.3 | | |
| D0 to D7, vaccine-related systemic AE | 33.3 | 34 | | |
| D0 to D7, vaccine-related solicited systemic AE | 31.3 | 32.9 | | |
| D0 to D7, vaccine-related unsolicited systemic AE | 3.1 | 2.9 | | |
| D8 to D28, any AE | 10.7 | 11 | | |
| D8 to D28, ISR | 0 | 0 | | |
| D8 to D28, systemic AE | 10.7 | 11 | | |
| D8 to D28, vaccine-related systemic AE | 1.3 | 0.5 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects reporting solicited injection-site reactions from D0 to D7 after one dose of REVAXIS vaccine or DT Polio vaccine

| | |
|-----------------|---|
| End point title | Proportion of subjects reporting solicited injection-site reactions from D0 to D7 after one dose of REVAXIS vaccine or DT Polio vaccine |
|-----------------|---|

End point description:

Solicited injection-site adverse reactions (ISRs: injection-site pain, injection-site erythema, and injection-site swelling) were reported onto the diary card by the parent(s) or legal representative from day 0 (D0) to D7.

AEs at injection sites were always considered as related to vaccine (Injection-Site Reactions (ISRs)).

Descriptive analysis was done on the Safety Analysis set.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| One month (28 to 35 days) after vaccination | |

| End point values | REVAXIS Group | DT Polio Group | | |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 384 | 374 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Injection site erythema | 40.9 | 47.1 | | |
| Injection site pain | 69.8 | 69.8 | | |
| Injection site swelling | 32.3 | 37.4 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects reporting solicited systemic adverse events and reactions from D0 to D7 after one dose of REVAXIS vaccine or DT Polio vaccine

| | |
|-----------------|--|
| End point title | Proportion of subjects reporting solicited systemic adverse events and reactions from D0 to D7 after one dose of REVAXIS vaccine or DT Polio vaccine |
|-----------------|--|

End point description:

Solicited systemic adverse events (AEs: headache, myalgia, pyrexia) were reported onto the diary card by the parent(s) or legal representative from day 0 (D0) to D7.

The investigator had to assess whether systemic AEs were related or not to the vaccine. All (related and unrelated) are displayed here.

Pyrexia was defined in this study as an oral temperature of 37.5°C or over. From D0 to D7, temperature values were captured in the diary card. In case of an oral temperature of 37.5°C or over at D7, the maximum temperature value of the event was also captured. From D0 to D7, temperature had to be measured once daily at the same time every day, preferably in the evening, and at the time of any apparent fever. At any time during the study, the highest observed temperature of the day had to be recorded in the diary card.

Descriptive analysis was done on the Safety Analysis set.

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

End point timeframe:

One month (28 to 35 days) after vaccination

| End point values | REVAXIS Group | DT Polio Group | | |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 384 | 374 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Headache (all) | 15.1 | 19.3 | | |
| Headache (related) | 12.2 | 16.6 | | |
| Myalgia (all) | 21.4 | 17.9 | | |
| Myalgia (related) | 19.3 | 17.1 | | |

| | | | | |
|-------------------|------|------|--|--|
| Pyrexia (all) | 11.2 | 14.4 | | |
| Pyrexia (related) | 9.6 | 11.2 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event (AE) data were collected from Day 0 (D0) to Visit 2 (D28 to D35).

Solicited AEs (collected from D0 to D7) are detailed in the "End points" section.

Unsolicited AEs (collected from D0 to D28) are detailed in this section.

Adverse event reporting additional description:

One subject was randomised in the DT Polio Group but received REVAXIS vaccine. The subject was thus included in the REVAXIS Group in the Safety Analysis set, which therefore included 384 subjects in the REVAXIS group, and 374 subjects in the DT Polio Group.

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

Dictionary used

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

| | |
|--------------------|-----|
| Dictionary version | 9.1 |
|--------------------|-----|

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | REVAXIS Group |
|-----------------------|---------------|

Reporting group description:

Participants received a single dose of REVAXIS (diphtheria, tetanus and poliomyelitis (inactivated) vaccine (adsorbed, reduced antigen(s) content)).

The number of subjects reporting at least 1 unsolicited ISR or AE with incidence $\geq 1\%$ are presented hereafter. If each unsolicited ISR or AE with incidence $\geq 1\%$ was reported by a different subject, the number of subjects reporting at least 1 unsolicited ISR or AE with incidence $\geq 1\%$ would have been 67.

| | |
|-----------------------|----------------|
| Reporting group title | DT Polio Group |
|-----------------------|----------------|

Reporting group description:

Participants received a single dose of DT Polio (diphtheria, tetanus and inactivated poliovirus vaccine).

The number of subjects reporting at least 1 unsolicited ISR or AE with incidence $\geq 1\%$ are presented hereafter. If each unsolicited ISR or AE with incidence $\geq 1\%$ was reported by a different subject, the number of subjects reporting at least 1 unsolicited ISR or AE with incidence $\geq 1\%$ would have been 59.

| Serious adverse events | REVAXIS Group | DT Polio Group | |
|---|---|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 384 (0.00%) | 1 / 374 (0.27%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Surgical and medical procedures | | | |
| Nose fracture | Additional description: Subject 9500002 experienced accidental severe nose fracture 14 days after receiving one dose of DT Polio vaccine. He was hospitalised to treat the fracture by surgery. SAE assessed as unrelated with the study vaccine. | | |
| subjects affected / exposed | 0 / 384 (0.00%) | 1 / 374 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| Non-serious adverse events | REVAXIS Group | DT Polio Group | |
|---|-------------------|-------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 67 / 384 (17.45%) | 59 / 374 (15.78%) | |
| Nervous system disorders | | | |
| D8-D28, Headache | | | |
| subjects affected / exposed | 5 / 384 (1.30%) | 2 / 374 (0.53%) | |
| occurrences (all) | 6 | 2 | |
| General disorders and administration site conditions | | | |
| D8-D28, Pyrexia | | | |
| subjects affected / exposed | 6 / 384 (1.56%) | 4 / 374 (1.07%) | |
| occurrences (all) | 7 | 4 | |
| D0-D7, Pruritus | | | |
| subjects affected / exposed | 5 / 384 (1.30%) | 11 / 374 (2.94%) | |
| occurrences (all) | 5 | 11 | |
| Gastrointestinal disorders | | | |
| D0-D7, Abdominal pain | | | |
| subjects affected / exposed | 4 / 384 (1.04%) | 8 / 374 (2.14%) | |
| occurrences (all) | 4 | 8 | |
| D0-D7, Vomiting | | | |
| subjects affected / exposed | 4 / 384 (1.04%) | 4 / 374 (1.07%) | |
| occurrences (all) | 4 | 4 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| D0-D7, Cough | | | |
| subjects affected / exposed | 8 / 384 (2.08%) | 6 / 374 (1.60%) | |
| occurrences (all) | 8 | 6 | |
| D8-D28, Cough | | | |
| subjects affected / exposed | 6 / 384 (1.56%) | 3 / 374 (0.80%) | |
| occurrences (all) | 7 | 3 | |
| Infections and infestations | | | |
| D8-D28, Ear infection | | | |
| subjects affected / exposed | 3 / 384 (0.78%) | 7 / 374 (1.87%) | |
| occurrences (all) | 3 | 7 | |
| D8-D28, Gastroenteritis | | | |
| subjects affected / exposed | 1 / 384 (0.26%) | 4 / 374 (1.07%) | |
| occurrences (all) | 1 | 4 | |
| D8-D28, Nasopharyngitis | | | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 5 / 384 (1.30%) | 0 / 374 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| D0-D7, Rhinitis | | | |
| subjects affected / exposed | 7 / 384 (1.82%) | 5 / 374 (1.34%) | |
| occurrences (all) | 7 | 5 | |
| D8-D28, Pharyngitis | | | |
| subjects affected / exposed | 5 / 384 (1.30%) | 2 / 374 (0.53%) | |
| occurrences (all) | 5 | 2 | |
| D0-D7, Tonsillitis | | | |
| subjects affected / exposed | 4 / 384 (1.04%) | 1 / 374 (0.27%) | |
| occurrences (all) | 4 | 1 | |
| D8-D28, Tonsillitis | | | |
| subjects affected / exposed | 4 / 384 (1.04%) | 2 / 374 (0.53%) | |
| occurrences (all) | 4 | 2 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 06 March 2007 | Administrative changes |
| 31 May 2007 | Extension of the recruitment period for 4 additional months |
| 13 July 2007 | Opening of 6 new sites and closure of 6 inactive sites |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported