



Clinical trial results:

A Phase II, open-label trial to evaluate the safety, tolerability and antiviral activity of TMC125 in antiretroviral experienced HIV-1 infected children and adolescents

Summary

| | |
|--------------------------|-------------------------|
| EudraCT number | 2007-007086-21 |
| Trial protocol | GB DE BE PT ES FR NL IT |
| Global end of trial date | 30 August 2011 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 |
| This version publication date | 06 July 2016 |
| First version publication date | 16 May 2015 |

Trial information

Trial identification

| | |
|-----------------------|--------------------|
| Sponsor protocol code | TMC125-TiDP35-C213 |
|-----------------------|--------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00665847 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Janssen Research & Development |
| Sponsor organisation address | Archimedsweg 29-2333CM, Leiden, Netherlands, B235-0 |
| Public contact | Janssen Research & Development, Clinical Registry Group, ClinicalTrialsEU@its.jnj.com |
| Scientific contact | Janssen Research & Development, Clinical Registry Group, ClinicalTrialsEU@its.jnj.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-000222-PIP01-08 |
| 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 | 30 August 2011 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 August 2011 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate safety and tolerability of etravirine in combination with other antiretroviral (ARVs) over a 24-week treatment period in children and adolescents.

Protection of trial subjects:

The safety assessments included laboratory measurements (for example hematology and coagulation, biochemistry, urinalysis, hepatitis serology/Viremia), cardiovascular safety, vital sign measurements and electrocardiograms (ECGs). Adverse events and vital signs were monitored throughout the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 06 August 2008 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Argentina: 15 |
| Country: Number of subjects enrolled | Brazil: 9 |
| Country: Number of subjects enrolled | Canada: 4 |
| Country: Number of subjects enrolled | Spain: 7 |
| Country: Number of subjects enrolled | France: 3 |
| Country: Number of subjects enrolled | United Kingdom: 1 |
| Country: Number of subjects enrolled | Italy: 7 |
| Country: Number of subjects enrolled | Puerto Rico: 1 |
| Country: Number of subjects enrolled | Portugal: 5 |
| Country: Number of subjects enrolled | Romania: 4 |
| Country: Number of subjects enrolled | Thailand: 20 |
| Country: Number of subjects enrolled | United States: 15 |
| Country: Number of subjects enrolled | South Africa: 10 |
| Worldwide total number of subjects | 101 |
| EEA total number of subjects | 27 |

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) | 41 |
| Adolescents (12-17 years) | 60 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

In total, 41 investigators in 13 countries enrolled participants in study TMC125-C213.

Pre-assignment

Screening details:

A total of 103 participants were documented as being enrolled in the study, however 2 participants were randomized in error. Therefore, 101 participants were enrolled and treated with etravirine (ETR) also known as TMC125 and included in the intent-to-treat (ITT) population.

Period 1

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

Arms

| | |
|-----------|--------|
| Arm title | TMC125 |
|-----------|--------|

Arm description:

TMC125 dosed according to body weight (kilogram) from 100 milligram (mg) to 200 mg twice a day

| | |
|--|---------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | TMC125 |
| Investigational medicinal product code | TMC125 (formulation F060) |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

TMC125 dosed according to body weight (kilogram) from 100 milligram (mg) to 200 mg twice a day

| Number of subjects in period 1 | TMC125 |
|--|--------|
| Started | 101 |
| Completed | 76 |
| Not completed | 25 |
| Consent withdrawn by subject | 2 |
| Adverse event | 8 |
| Resistance to TMC125 | 1 |
| Switch to commercial medication | 1 |
| Subject reached a virologic endpoint | 4 |
| Subject non-compliant | 8 |
| Subject ineligible to continue the trial | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | TMC125 |
|-----------------------|--------|

Reporting group description:

TMC125 dosed according to body weight (kilogram) from 100 milligram (mg) to 200 mg twice a day

| Reporting group values | TMC125 | Total | |
|---|--------|-------|--|
| Number of subjects | 101 | 101 | |
| Title for AgeCategorical Units: subjects | | | |
| Children (2-11 years) | 41 | 41 | |
| Adolescents (12-17 years) | 60 | 60 | |
| Adults (18-64 years) | 0 | 0 | |
| From 65 to 84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Title for AgeContinuous Units: years | | | |
| arithmetic mean | 12.2 | | |
| standard deviation | ± 2.99 | - | |
| Title for Gender Units: subjects | | | |
| Female | 64 | 64 | |
| Male | 37 | 37 | |

End points

End points reporting groups

| | |
|--|--------|
| Reporting group title | TMC125 |
| Reporting group description: | |
| TMC125 dosed according to body weight (kilogram) from 100 milligram (mg) to 200 mg twice a day | |

Primary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs)

| | |
|-----------------|--|
| End point title | Number of Participants With Treatment-Emergent Adverse Events (TEAEs) ^[1] |
|-----------------|--|

End point description:

A treatment-emergent adverse event (TEAE) was defined as an event that occurred in the 48-week treatment period during which it emerged (i.e. started or worsened in severity, relation, or other attribute), and not in the subsequent study periods, even if the event continued to be present. Adverse events were graded from 1 to 4 in severity using the Division of Acquired Immunodeficiency Syndrome severity scale (grade 1 being less severe and grade 4 being more severe). ETR=etravirine/TMC125; OBR=optimized background regimen

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

End point timeframe:

48 weeks

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 statistics were done, no inferential statistical analyses were performed.

| End point values | TMC125 | | | |
|--|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 101 | | | |
| Units: Participants | | | | |
| Any TEAE | 89 | | | |
| TEAEs that were fatal | 0 | | | |
| TEAEs that were serious | 5 | | | |
| TEAEs that were grade 3 or 4 in severity | 14 | | | |
| TEAEs leading to temporary ETR discontinuation | 8 | | | |
| TEAEs leading to permanent ETR discontinuation | 8 | | | |
| TEAEs possibly related to ETR | 23 | | | |
| TEAEs probably related to ETR | 14 | | | |
| TEAEs very likely related to ETR | 3 | | | |
| TEAEs at least possibly related to ETR | 33 | | | |
| TEAEs possibly related to OBR | 27 | | | |
| TEAEs probably related to OBR | 12 | | | |
| TEAEs very likely related to OBR | 5 | | | |
| TEAEs at least possibly related to OBR | 36 | | | |
| TEAEs of at least grade 2 in severity | 21 | | | |
| TEAEs of at least grade 3 in severity | 3 | | | |
| TEAEs of interest: Skin event | 31 | | | |
| TEAEs of interest: Rash | 23 | | | |
| TEAEs of interest: severe cutaneous reactions | 7 | | | |

| | | | | |
|--|---|--|--|--|
| TEAEs of interest: angioedema | 4 | | | |
| TEAEs of interest: neuropsychiatric events | 2 | | | |
| TEAEs of interest: hepatic events | 0 | | | |
| TEAEs of interest: cardiac events | 0 | | | |
| TEAEs of interest: bleeding events | 0 | | | |
| TEAEs of interest: pancreatic events | 1 | | | |
| TEAEs of interest: lipid-related events | 6 | | | |
| TEAEs of interest: neoplasms | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Treatment-Emergent Adverse Events (TEAEs)

| | |
|-----------------|--|
| End point title | Percentage of Participants With Treatment-Emergent Adverse Events (TEAEs) ^[2] |
|-----------------|--|

End point description:

The percentage of participants with a treatment-emergent adverse event (TEAE) (defined as an event that occurred in the 48-week treatment period during which it emerged [i.e. started or worsened in severity, relation, or other attribute], and not in the subsequent study periods, even if the event continued to be present] are provided below. Adverse events were graded from 1 to 4 in severity using the Division of Acquired Immunodeficiency Syndrome severity scale (grade 1 being less severe and grade 4 being more severe). ETR=etravirine/TMC125; OBR=optimized background regimen.

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

End point timeframe:

48 weeks

Notes:

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

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

| End point values | TMC125 | | | |
|--|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 101 | | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| Any TEAE | 88.1 | | | |
| TEAEs that were fatal | 0 | | | |
| TEAEs that were serious | 5 | | | |
| TEAEs that were grade 3 or 4 in severity | 13.9 | | | |
| TEAEs leading to temporary ETR discontinuation | 7.9 | | | |
| TEAEs leading to permanent ETR discontinuation | 7.9 | | | |
| TEAEs possibly related to ETR | 22.8 | | | |
| TEAEs probably related to ETR | 13.9 | | | |
| TEAEs very likely related to ETR | 3 | | | |
| TEAEs at least possibly related to ETR | 32.7 | | | |
| TEAEs possibly related to OBR | 26.7 | | | |
| TEAEs probably related to OBR | 11.9 | | | |

| | | | | |
|---|------|--|--|--|
| TEAEs very likely related to OBR | 5 | | | |
| TEAEs at least possibly related to OBR | 35.6 | | | |
| TEAEs of at least grade 2 in severity | 20.8 | | | |
| TEAEs of at least grade 3 in severity | 3 | | | |
| TEAEs of interest: Skin event | 30.7 | | | |
| TEAEs of interest: Rash | 22.8 | | | |
| TEAEs of interest: severe cutaneous reactions | 6.9 | | | |
| TEAEs of interest: angioedema | 4 | | | |
| TEAEs of interest: neuropsychiatric events | 2 | | | |
| TEAEs of interest: hepatic events | 0 | | | |
| TEAEs of interest: cardiac events | 0 | | | |
| TEAEs of interest: bleeding events | 0 | | | |
| TEAEs of interest: pancreatic events | 1 | | | |
| TEAEs of interest: lipid-related events | 5.9 | | | |
| TEAEs of interest: neoplasms | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve Over 12 Hours at Steady-state (AUC12h) of Etravirine

| | |
|------------------------|--|
| End point title | Area Under the Plasma Concentration-Time Curve Over 12 Hours at Steady-state (AUC12h) of Etravirine |
| End point description: | The AUC12h is a Bayesian estimation based on a population pharmacokinetic model and sparse samples collected at each visit over the duration of trial. For each sparse sample taken, the time blood sample was recorded as well as the time of etravirine intake just prior to the time of blood sample. |
| End point type | Secondary |
| End point timeframe: | Weeks 4-48 |

| | | | | |
|--------------------------------------|-----------------|--|--|--|
| End point values | TMC125 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 101 | | | |
| Units: ng.h/mL | | | | |
| arithmetic mean (standard deviation) | 5216 (± 4305) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Plasma Concentration (C0h) of Etravirine

| | |
|---|---|
| End point title | Trough Plasma Concentration (C0h) of Etravirine |
| End point description: | |
| Trough plasma concentration is the plasma concentration before dosing or at the end of the dosing interval of any dose other than the first dose. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 48 | |

| | | | | |
|--------------------------------------|-----------------|--|--|--|
| End point values | TMC125 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 101 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | 346 (± 342) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (Cmax) of Etravirine

| | |
|--|---|
| End point title | Maximum Plasma Concentration (Cmax) of Etravirine |
| End point description: | |
| Etravirine/TMC125 (ETR) Cmax was approximated for each individual using the median value of plasma ETR concentrations taken 4 hours postdose (± 1 hour), when available, on the day of the Week 4 visit. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 4 | |

| | | | | |
|--------------------------------------|-----------------|--|--|--|
| End point values | TMC125 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 66 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | 589 (± 486) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Virologic Response at Week 24

| | |
|---|---|
| End point title | Percentage of Participants With Virologic Response at Week 24 |
| End point description: | |
| Virologic response was defined as the percentage of participants with plasma viral load less than (<) 50 | |

copies/ milliliter (mL) at Week 24 calculated according to the non-completer=failure (NC=F) imputation method.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 24 | |

| | | | | |
|-----------------------------------|-----------------|--|--|--|
| End point values | TMC125 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 101 | | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 52.5 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Human Immunodeficiency Virus – Type 1 (HIV-1) Ribonucleic Acid (RNA) in Plasma Over Time

| | |
|------------------------|--|
| End point title | Change From Baseline in Human Immunodeficiency Virus – Type 1 (HIV-1) Ribonucleic Acid (RNA) in Plasma Over Time |
| End point description: | Human Immunodeficiency Virus – Type 1 (HIV-1) Ribonucleic Acid (RNA) in Plasma were analyzed. |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 48 | |

| | | | | |
|----------------------------------|-----------------|--|--|--|
| End point values | TMC125 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 101 | | | |
| Units: log10 copies/mL | | | | |
| arithmetic mean (standard error) | -1.53 (± 0.132) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Cell Counts Over Time

| | |
|------------------------|--|
| End point title | Change From Baseline in CD4 Cell Counts Over Time |
| End point description: | CD4 cells (a type of white blood cells) are circulating in blood and gives an idea of how strong the HIV positive person's immune system really is. The values of CD4 cell counts were analyzed. |

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 48 | |

| | | | | |
|----------------------------------|-----------------|--|--|--|
| End point values | TMC125 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 101 | | | |
| Units: 10E6 cells/L | | | | |
| arithmetic mean (standard error) | 156 (± 22.7) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: The Emergence of Non-Nucleoside Reverse Transcriptase Inhibitor Resistance-Associated Mutations (NNRTI RAMs) in Participants Classified as Virologic Failures

| | |
|-----------------|---|
| End point title | The Emergence of Non-Nucleoside Reverse Transcriptase Inhibitor Resistance-Associated Mutations (NNRTI RAMs) in Participants Classified as Virologic Failures |
|-----------------|---|

End point description:

Virologic failure (lack of response) was defined as: plasma viral load decline of < 0.5 log₁₀ from Baseline by Week 8 and/or plasma viral load decline of <1.0 log₁₀ from Baseline by Week 12. Virologic failure (loss of response) was defined as 2 consecutive measurements of plasma viral load greater than (>) 0.5 log₁₀ above the nadir after a minimum of 12 weeks of treatment. The table below provides data for 41 virologic failures of which 30 had mutation data available. In the table below, only the 4 most frequently emerging mutations are presented (emerging in at least 3 patients).

| | |
|---------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Endpoint (up to Week 48) | |

| | | | | |
|-----------------------------|-----------------|--|--|--|
| End point values | TMC125 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: Participants | | | | |
| V90I | 3 | | | |
| L100I | 3 | | | |
| E138A | 3 | | | |
| Y181C | 8 | | | |

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 52

Adverse event reporting additional description:

Only participants who had at least one of the TEAEs listed in the Other (non Serious) AE table are included in the Total no. participants with Non-Serious Adverse Events.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 11.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | TMC125 |
|-----------------------|--------|

Reporting group description:

TMC125 dosed according to body weight (kilogram) from 100 milligram (mg) to 200 mg twice a day

| Serious adverse events | TMC125 | | |
|---|-----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 101 (4.95%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Investigations | | | |
| Immunoglobulins | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lymphocyte morphology abnormal | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Drug toxicity | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 1 / 101 (0.99%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Overdose | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Drug resistance | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Ulcerative keratitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Social circumstances | | | |
| Treatment noncompliance | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | | |
| 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 | TMC125 | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 70 / 101 (69.31%) | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 9 / 101 (8.91%) | | |
| occurrences (all) | 12 | | |
| General disorders and administration site conditions | | | |

| | | | |
|---|--|--|--|
| Pyrexia subjects affected / exposed occurrences (all) | 9 / 101 (8.91%) 10 | | |
| Eye disorders Conjunctivitis subjects affected / exposed occurrences (all) | 6 / 101 (5.94%) 6 | | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) | 16 / 101 (15.84%) 18 10 / 101 (9.90%) 11 11 / 101 (10.89%) 11 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) | 13 / 101 (12.87%) 18 6 / 101 (5.94%) 10 | | |
| Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) Rash maculo-papular subjects affected / exposed occurrences (all) | 11 / 101 (10.89%) 12 9 / 101 (8.91%) 10 | | |
| Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Oral herpes | 9 / 101 (8.91%) 10 | | |

| | | | |
|-----------------------------------|-------------------|--|--|
| subjects affected / exposed | 6 / 101 (5.94%) | | |
| occurrences (all) | 8 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 8 / 101 (7.92%) | | |
| occurrences (all) | 11 | | |
| Rhinitis | | | |
| subjects affected / exposed | 6 / 101 (5.94%) | | |
| occurrences (all) | 8 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 27 / 101 (26.73%) | | |
| occurrences (all) | 41 | | |
| Sinusitis | | | |
| subjects affected / exposed | 6 / 101 (5.94%) | | |
| occurrences (all) | 9 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 04 September 2008 | The overall reason for the amendment was to address feedback provided by the United States Food and Drug Administration (US FDA) and modify inclusive criterion. |
| 30 January 2009 | The overall reason for the amendment was to modify inclusion criterion. |
| 24 March 2010 | The overall reason for the amendment was to adjust body weight criterion, definition Serious Adverse Events (SAE) and criterion regarding co-enrollment of participants in another study. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported