# Clinical trial results:
# EVINEC: Safety and Tolerability of Everolimus as second-line treatment in poorly differentiated neuroendocrine carcinoma / neuroendocrine carcinoma G3 according to WHO 2010 and neuroendocrine tumor G3 - an investigtor initiated Phase II study.

## Summary

| | |
|---|---|
| EudraCT number | 2012-004550-28 |
| Trial protocol | DE |
| Global end of trial date | 04 May 2020 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 01 November 2022 |
| First version publication date | 01 November 2022 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | AIO-NET-0112 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02113800 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Novartis-Nr: : CRAD001KDE55T |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | AIO-Studien-gGmbH |
| Sponsor organisation address | Kuno-Fischer-Str. 8, Berlin, Germany, 14057 |
| Public contact | AIO-Studien-gGmbH, AIO-Studien-gGmbH, +49 30814534431, info@aio-studien-ggmbh.de |
| Scientific contact | AIO-Studien-gGmbH, AIO-Studien-gGmbH, +49 30814534431, info@aio-studien-ggmbh.de |

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? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 07 September 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 04 May 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 04 May 2020 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate tolerability and safety of everolimus in second-line treatment of poorly differentiated neuroendocrine carcinoma / neuroendocrine carcinoma G3 according to WHO 2010 and neuroendocrine tumors G3. Safety and tolerability of Everolimus can be inferred if type, frequency and seriousness of observed AEs is comparable to those determined in previous Everolimus trials in NET (Radiant-1,2 and 3).

Protection of trial subjects:

This study was planned, analyzed and conducted according to the study protocol and in accordance with the International Conference on Harmonization (ICH) ‚Guideline for Good Clinical Practice E6(R1)‘, CPMP/ICH/135/95, based on the principles of the Declaration of Helsinki (1964) and its October 1996 amendment (Somerset West, South Africa). The study was duly conducted in compliance with the German Arzneimittelgesetz (AMG; German Drug Law), and the corresponding Directive 2001/20/EC. Subjects were fully informed regarding all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 01 March 2015 |
| 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 | Germany: 39 |
| Worldwide total number of subjects | 39 |
| EEA total number of subjects | 39 |

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) | 0 |
| Adolescents (12-17 years) | 0 |

| | |
|---|---|
| Adults (18-64 years) | 28 |
| From 65 to 84 years | 11 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

42 patients were screened for study participation, 39 of whon were found eligible.

### Period 1

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

### Arms

| | |
|---|---|
| **Arm title** | Everolimus 10 mg/d |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Everolimus |
| Investigational medicinal product code | |
| Other name | Afinitor |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

A dose of 10 mg was to be administered orally once daily at the same time every day, consistently either with or without food, swallowed whole with a glass of water.

| **Number of subjects in period 1** | Everolimus 10 mg/d |
|---|---|
| Started | 39 |
| Completed | 39 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Treatment |

Reporting group description: -

| Reporting group values | Treatment | Total | |
|---|---|---|---|
| Number of subjects | 39 | 39 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | | 0 | |
| Newborns (0-27 days) | | 0 | |
| Infants and toddlers (28 days-23 months) | | 0 | |
| Children (2-11 years) | | 0 | |
| Adolescents (12-17 years) | | 0 | |
| Adults (18-64 years) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous<br>Units: years | | | |
| median | 57.0 | | |
| full range (min-max) | 33 to 77 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 16 | 16 | |
| Male | 23 | 23 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Everolimus 10 mg/d |
| Reporting group description: - | |
| Subject analysis set title | Per protocol |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Of 39 treated patients, 9 were excluded from the per protocol analysis set. Reasons were the retroactive histological tumor diagnosis as non-NEN by central pathology (3 patients), and major protocol violations (6 patients).

### Primary: Overall survival

| | |
|---|---|
| End point title | Overall survival[1] |

End point description:

Primary objective of this study was limted to safety and tolerability. Hence, no primary efficacy endpoint was definded. One of the secondary endpoints, overall survival (OS), is given instead.

The median OS was 12.0 months for all NEN G3 patients together (95%-CI 7.0-23-9). A lower OS occurred in NEC G3 patients with 5.6 months (95%-CI 1.3-20.1) and for MANEC patients with 7.0 months (95%-CI 1.0-11.1) compared to NET G3 patients with 23.9 months (95%-CI 12.0-NC).

OS rate at 12 months in the PP Population was 49.0% (95%-CI 30.2%-65.4%). OS at 12 months was lowest in MANEC patients with 14.3% (95%-CI 0.7%-46.5%) and in NEC G3 patients with 30.0% (95%-CI 7.1%-57.8%) compared to NET G3 patients with 83.9% (95%-CI 49.4%-95.7%).

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

End point timeframe:

Overall survival (OS) was defined as the time from the date of first treatment to the date of death. Patients for whom not date of death was recorded were censored at the date of last contact.

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: Since the study had no primary efficacy endpoint, OS is given for this data field instead. No in-depth statistical analysis was perfomed.

| End point values | Per protocol | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 30 | | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 12.0 (7.0 to 23.9) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Progression-free survival

| | |
|---|---|
| End point title | Progression-free survival |

End point description:

The median progressive free survival (PFS) was 2.2 months for all NEN G3 patients together (95%-CI 1.8-4.8).
PFS was shorter in NEC G3 with a median of 1.8 months (95% CI 0.9-2.0) and in MANEC with 2.2 months (95% CI 0.7-4.1) as compared to NET G3 patients with 5.2 months (95% CI 1.6-7.3).

PFS rate at 6 months was lowest in MANEC patients with 14.3% (95%-CI 0.7%-46.5%) and NEC G3 patients with
20.0% (95%-CI 3.1%-47.5%) compared to NET G3 patients with 41.7% (95%-CI 15.2%-66.5%).

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

End point timeframe:

Progression-Free Survival (PFS) was defined as the time from first treatment to PD or death. Patients who had no PD and did not die were censored at the time of the last tumor assessment.

| **End point values** | Everolimus 10 mg/d | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 30 | | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 2.2 (1.8 to 4.8) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Best overall response, ORR and DCR

| End point title | Best overall response, ORR and DCR |
|---|---|

End point description:

Partial remission was observed for one patient, resulting in an Objective Response Rate (ORR) of 3.3%, [95%CI 0.6%-16.7%].

Disease control was documented for 14 NEN G3 patients, resulting in a disease control rate (DCR) of 46.7% [95%CI 30.2%-63.9%].

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

End point timeframe:

Best response among all available response assessments

| **End point values** | Everolimus 10 mg/d | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 30 | | | |
| Units: CR, PR, SD and PD | | | | |
| Complete Remission (CR) | 0 | | | |
| Partial Remission (PR) | 1 | | | |
| Stable Disease (SD) | 13 | | | |
| Progressive Disease (PD) | 13 | | | |
| No assessment | 3 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Reporting of all adverse events started at the first treatment visit and ended on the EoT visit.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 23 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Everolimus 10 mg/d |

Reporting group description: -

| Serious adverse events | Everolimus 10 mg/d | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | | |
| number of deaths (all causes) | 29 | | |
| number of deaths resulting from adverse events | | | |
| Investigations | | | |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Radiation pneumonitis | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|---|---|---|
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Pain | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Melaena | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Influenza | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| 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** | Everolimus 10 mg/d | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 39 / 39 (100.00%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |

| | | | |
|---|---|---|---|
| Tumor pain | | | |
| subjects affected / exposed | 4 / 39 (10.26%) | | |
| occurrences (all) | 6 | | |
| Vascular disorders | | | |
| Lymphoedema | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | | |
| occurrences (all) | 2 | | |
| General disorders and administration site conditions | | | |
| Chills | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | | |
| occurrences (all) | 5 | | |
| Fatigue | | | |
| subjects affected / exposed | 14 / 39 (35.90%) | | |
| occurrences (all) | 16 | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | | |
| occurrences (all) | 5 | | |
| Influenza like illness | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | | |
| occurrences (all) | 4 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | | |
| occurrences (all) | 6 | | |
| Pain | | | |
| subjects affected / exposed | 6 / 39 (15.38%) | | |
| occurrences (all) | 7 | | |
| Pyrexia | | | |
| subjects affected / exposed | 6 / 39 (15.38%) | | |
| occurrences (all) | 6 | | |
| Swelling face | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | | |
| occurrences (all) | 2 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | | |
| occurrences (all) | 3 | | |

| | | | |
|---|---|---|---|
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all) | 4 / 39 (10.26%)<br>5 | | |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all) | 8 / 39 (20.51%)<br>9 | | |
| Pneumonitis<br>subjects affected / exposed<br>occurrences (all) | 2 / 39 (5.13%)<br>3 | | |
| Psychiatric disorders<br>Anxiety<br>subjects affected / exposed<br>occurrences (all) | 2 / 39 (5.13%)<br>2 | | |
| Depression<br>subjects affected / exposed<br>occurrences (all) | 2 / 39 (5.13%)<br>2 | | |
| Insomnia<br>subjects affected / exposed<br>occurrences (all) | 2 / 39 (5.13%)<br>2 | | |
| Investigations<br>Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 2 / 39 (5.13%)<br>2 | | |
| C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all) | 4 / 39 (10.26%)<br>4 | | |
| Gamma-glutamyltransferase increased<br>subjects affected / exposed<br>occurrences (all) | 2 / 39 (5.13%)<br>2 | | |
| Platelet count decreased<br>subjects affected / exposed<br>occurrences (all) | 4 / 39 (10.26%)<br>7 | | |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all) | 6 / 39 (15.38%)<br>8 | | |
| Cardiac disorders | | | |

| | | | |
|---|---|---|---|
| Angina pectoris | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | | |
| occurrences (all) | 2 | | |
| Atrial tachycardia | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences (all) | 1 | | |
| Atrioventricular block | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | | |
| occurrences (all) | 3 | | |
| Dysgeusia | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | | |
| occurrences (all) | 3 | | |
| Headache | | | |
| subjects affected / exposed | 4 / 39 (10.26%) | | |
| occurrences (all) | 4 | | |
| Paraesthesia | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | | |
| occurrences (all) | 2 | | |
| Taste disorder | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | | |
| occurrences (all) | 2 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | | |
| occurrences (all) | 5 | | |
| Anaemia of malignant disease | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences (all) | 1 | | |
| Increased tendency to bruise | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences (all) | 1 | | |
| Lymphadenopathy | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 39 (5.13%) | | |
| occurrences (all) | 2 | | |
| Lymphopenia | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | | |
| occurrences (all) | 2 | | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences (all) | 1 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | | |
| occurrences (all) | 2 | | |
| Ear and labyrinth disorders | | | |
| Tinnitus | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences (all) | 1 | | |
| Vertigo | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | | |
| occurrences (all) | 2 | | |
| Eye disorders | | | |
| Eye swelling | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences (all) | 1 | | |
| Visual impairment | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| Abdominal hernia | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences (all) | 1 | | |
| Abdominal mass | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences (all) | 1 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 9 / 39 (23.08%) | | |
| occurrences (all) | 11 | | |
| Abdominal pain lower | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences (all) | 1 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | | |
| occurrences (all) | 5 | | |
| Aphthous ulcer | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | | |
| occurrences (all) | 5 | | |
| Constipation | | | |
| subjects affected / exposed | 6 / 39 (15.38%) | | |
| occurrences (all) | 10 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 11 / 39 (28.21%) | | |
| occurrences (all) | 14 | | |
| Dry mouth | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | | |
| occurrences (all) | 5 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | | |
| occurrences (all) | 6 | | |
| Nausea | | | |
| subjects affected / exposed | 14 / 39 (35.90%) | | |
| occurrences (all) | 14 | | |
| Stomatitis | | | |
| subjects affected / exposed | 16 / 39 (41.03%) | | |
| occurrences (all) | 20 | | |
| Toothache | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | | |
| occurrences (all) | 3 | | |
| Vomiting | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | | |
| occurrences (all) | 9 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | | |
| occurrences (all) | 5 | | |

| | | | |
|---|---|---|---|
| Dry skin | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | | |
| occurrences (all) | 3 | | |
| Erythema | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | | |
| occurrences (all) | 3 | | |
| Erythema multiforme | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | | |
| occurrences (all) | 2 | | |
| Night sweats | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | | |
| occurrences (all) | 2 | | |
| Pruritus | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | | |
| occurrences (all) | 2 | | |
| Rash | | | |
| subjects affected / exposed | 7 / 39 (17.95%) | | |
| occurrences (all) | 8 | | |
| Renal and urinary disorders | | | |
| Nocturia | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | | |
| occurrences (all) | 3 | | |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | | |
| occurrences (all) | 3 | | |
| Back pain | | | |
| subjects affected / exposed | 7 / 39 (17.95%) | | |
| occurrences (all) | 9 | | |
| Flank pain | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | | |
| occurrences (all) | 2 | | |

| | | | |
|---|---|---|---|
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all) | 2 / 39 (5.13%)<br>3 | | |
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)<br>Uninary tract infection<br>subjects affected / exposed<br>occurrences (all) | <br>3 / 39 (7.69%)<br>3<br><br>4 / 39 (10.26%)<br>4 | | |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all)<br>Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)<br>Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)<br>Hypertriglyceridaemia<br>subjects affected / exposed<br>occurrences (all)<br>Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)<br>Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all)<br>Iron deficiency<br>subjects affected / exposed<br>occurrences (all) | <br>9 / 39 (23.08%)<br>10<br><br>2 / 39 (5.13%)<br>2<br><br>3 / 39 (7.69%)<br>4<br><br>2 / 39 (5.13%)<br>2<br><br>2 / 39 (5.13%)<br>2<br><br>3 / 39 (7.69%)<br>3<br><br>3 / 39 (7.69%)<br>3 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 10 August 2015 | Addition of IMP package sizes |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported