



Clinical trial results:

A Phase 3, Open-Label, Multicenter Study to Evaluate the Safety of Paricalcitol Capsules in Pediatric Subjects Ages 10 to 16 with Stage 5 Chronic Kidney Disease Receiving Peritoneal Dialysis or Hemodialysis

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2013-002610-13 |
| Trial protocol | PT DE GB |
| Global end of trial date | 24 April 2015 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 18 May 2016 |
| First version publication date | 18 May 2016 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | M11-612 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01382212 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | AbbVie |
| Sponsor organisation address | 1 North Waukegan Road, North Chicago, IL, United States, 60064 |
| Public contact | Global Medical Information, AbbVie, 001 800-633-9110, |
| Scientific contact | Ann Eldred, MD, AbbVie, ann.eldred@abbvie.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 | 24 April 2015 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 April 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to evaluate the safety of paricalcitol capsules for the treatment of secondary hyperparathyroidism in pediatric subjects ages 10 to 16 years with Stage 5 chronic kidney disease (CKD), receiving peritoneal dialysis or hemodialysis through the evaluation of the incidence of hypercalcemia.

Protection of trial subjects:

Subject and/or parent or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 03 October 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: 11 |
| Country: Number of subjects enrolled | Portugal: 1 |
| Country: Number of subjects enrolled | United Kingdom: 1 |
| Worldwide total number of subjects | 13 |
| EEA total number of subjects | 2 |

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) | 13 |
| Adults (18-64 years) | 0 |

| | |
|---------------------|---|
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 26 subjects were screened and 13 pediatric subjects (between 10 and 16 years of age) were enrolled; 1 subject was 16 years of age at the time of Screening and turned 17 by the time treatment began.

Period 1

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

Arms

| | |
|-----------|--------------|
| Arm title | Paricalcitol |
|-----------|--------------|

Arm description:

Open-label paricalcitol (maximum dose of 16 µg), 3 times weekly (no more frequently than every other day) for 12 weeks.

| | |
|--|---------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | paricalcitol 1 µg capsule, soft |
| Investigational medicinal product code | |
| Other name | ABT-358, Zemplar |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Starting dose of paricalcitol was determined by the intact parathyroid hormone (iPTH) value (iPTH/120) from prior to Day 1, rounded down to the nearest whole number, not to exceed 16 µg 3 times weekly, no more frequently than every other day. Decisions to hold, maintain, increase, or decrease a dose were based on the iPTH, phosphorus, and calcium results generated from the most recent visit and within target Kidney Dialysis Outcomes Quality Initiatives (KDOQI) levels.

| | |
|--|---------------------------------|
| Investigational medicinal product name | paricalcitol 2 µg capsule, soft |
| Investigational medicinal product code | |
| Other name | ABT-358, Zemplar |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Starting dose of paricalcitol was determined by the iPTH/120 from prior to Day 1, rounded down to the nearest whole number, not to exceed 16 µg 3 times weekly, no more frequently than every other day. Decisions to hold, maintain, increase, or decrease a dose were based on the iPTH, phosphorus, and calcium results generated from the most recent visit and within target KDOQI levels.

| Number of subjects in period 1 | Paricalcitol |
|--------------------------------|--------------|
| Started | 13 |
| Completed | 11 |
| Not completed | 2 |
| Withdrew consent | 1 |

| | |
|-------------------|---|
| Kidney transplant | 1 |
|-------------------|---|

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Paricalcitol |
|-----------------------|--------------|

Reporting group description:

Open-label paricalcitol (maximum dose of 16 µg), 3 times weekly (no more frequently than every other day) for 12 weeks.

| Reporting group values | Paricalcitol | Total | |
|---|----------------|-------|--|
| Number of subjects | 13 | 13 | |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | 14.5 ± 1.76 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 8 | 8 | |
| Male | 5 | 5 | |

End points

End points reporting groups

| | |
|---|--------------|
| Reporting group title | Paricalcitol |
| Reporting group description: Open-label paricalcitol (maximum dose of 16 µg), 3 times weekly (no more frequently than every other day) for 12 weeks. | |

Primary: Percentage of Subjects With Hypercalcemia

| | |
|---|--|
| End point title | Percentage of Subjects With Hypercalcemia ^[1] |
| End point description: The percentage of subjects with hypercalcemia, defined as at least 2 consecutive post-baseline corrected calcium values > 10.2 mg/dL (2.55 mmol/L). | |
| End point type | Primary |
| End point timeframe: Day 1 to Week 12 | |

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 data were summarized for this end point per protocol.

| End point values | Paricalcitol | | | |
|----------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 13 ^[2] | | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 15.3 (1.9 to 45.4) | | | |

Notes:

[2] - All-treated data set: all subjects enrolled and administered at least 1 dose of paricalcitol

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With 2 Consecutive iPTH/120 Between 150 and 300 pg/mL

| | |
|--|--|
| End point title | Percentage of Subjects With 2 Consecutive iPTH/120 Between 150 and 300 pg/mL |
| End point description: | |
| End point type | Secondary |
| End point timeframe: Baseline (last measurement collected prior to the first dose) to Week 12 | |

| | | | | |
|----------------------------------|---------------------|--|--|--|
| End point values | Paricalcitol | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 13 ^[3] | | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 38.5 (13.9 to 68.4) | | | |

Notes:

[3] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With 2 Consecutive iPTH Reductions of at Least 30% From Baseline

| | |
|-----------------|---|
| End point title | Percentage of Subjects With 2 Consecutive iPTH Reductions of at Least 30% From Baseline |
|-----------------|---|

End point description:

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

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Week 12

| | | | | |
|----------------------------------|---------------------|--|--|--|
| End point values | Paricalcitol | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 13 ^[4] | | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 61.5 (31.6 to 86.1) | | | |

Notes:

[4] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Hemoglobin: Mean Change from Baseline to Final Visit

| | |
|-----------------|--|
| End point title | Hemoglobin: Mean Change from Baseline to Final Visit |
|-----------------|--|

End point description:

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

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

| End point values | Paricalcitol | | | |
|--------------------------------------|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 ^[5] | | | |
| Units: g/dL | | | | |
| arithmetic mean (standard deviation) | -0.1 (± 1.263) | | | |

Notes:

[5] - All subjects in the all -treated data set with evaluable data

Statistical analyses

No statistical analyses for this end point

Secondary: Hematocrit: Mean Change from Baseline to Final Visit

| | |
|-----------------|--|
| End point title | Hematocrit: Mean Change from Baseline to Final Visit |
|-----------------|--|

End point description:

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

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

| End point values | Paricalcitol | | | |
|--------------------------------------|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 ^[6] | | | |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | -1.08 (± 5.066) | | | |

Notes:

[6] - All subjects in the all-treated data set with evaluable data

Statistical analyses

No statistical analyses for this end point

Secondary: Red Blood Cells: Mean Change from Baseline to Final Visit

| | |
|-----------------|---|
| End point title | Red Blood Cells: Mean Change from Baseline to Final Visit |
|-----------------|---|

End point description:

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

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

| End point values | Paricalcitol | | | |
|--------------------------------------|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 ^[7] | | | |
| Units: x10 ⁶ /μL | | | | |
| arithmetic mean (standard deviation) | -0.09 (± 0.496) | | | |

Notes:

[7] - All subjects in the all-treated data set with evaluable data

Statistical analyses

No statistical analyses for this end point

Secondary: White Blood Cells (WBC) and Platelet Count: Mean Change from Baseline to Final Visit

| | |
|-----------------|--|
| End point title | White Blood Cells (WBC) and Platelet Count: Mean Change from Baseline to Final Visit |
|-----------------|--|

End point description:

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

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

| End point values | Paricalcitol | | | |
|--------------------------------------|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 ^[8] | | | |
| Units: x10 ³ /μL | | | | |
| arithmetic mean (standard deviation) | | | | |
| WBC | -0.06 (± 2.982) | | | |
| Platelet Count | 19.2 (± 47.03) | | | |

Notes:

[8] - All subjects in the all-treated data set with evaluable data

Statistical analyses

No statistical analyses for this end point

Secondary: Neutrophils, Lymphocytes, Monocytes, Eosinophils, and Basophils: Mean Change from Baseline to Final Visit

| | |
|-----------------|---|
| End point title | Neutrophils, Lymphocytes, Monocytes, Eosinophils, and Basophils: Mean Change from Baseline to Final Visit |
|-----------------|---|

End point description:

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

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

| | | | | |
|--------------------------------------|-------------------|--|--|--|
| End point values | Paricalcitol | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 ^[9] | | | |
| Units: x10 ⁹ /μL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Neutrophils | 0.11 (± 2.6812) | | | |
| Lymphocytes | -0.294 (± 0.597) | | | |
| Monocytes | 0.032 (± 0.1276) | | | |
| Eosinophils | 0.059 (± 0.1522) | | | |
| Basophils | -0.01 (± 0.0322) | | | |

Notes:

[9] - All subjects in the all-treated data set with evaluable data

Statistical analyses

No statistical analyses for this end point

Secondary: Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Lactic Dehydrogenase (LDH), and Bone-Specific Alkaline Phosphatase (BSAP): Mean Change from Baseline to Final Visit

| | | | | |
|------------------------|---|--|--|--|
| End point title | Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Lactic Dehydrogenase (LDH), and Bone-Specific Alkaline Phosphatase (BSAP): Mean Change from Baseline to Final Visit | | | |
| End point description: | n=subjects with evaluable Baseline and Post-baseline data for each parameter. | | | |
| End point type | Secondary | | | |
| End point timeframe: | End point timeframe Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12) | | | |

| | | | | |
|--------------------------------------|--------------------|--|--|--|
| End point values | Paricalcitol | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 ^[10] | | | |
| Units: U/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| ALT (n=11) | -4.55 (± 16.501) | | | |
| AST (n=11) | -4.45 (± 12.25) | | | |
| LDH (n=11) | -6.5 (± 33.22) | | | |
| BSAP (n=9) | -49.4 (± 86.95) | | | |

Notes:

[10] - All subjects in the all-treated data set with evaluable data

Statistical analyses

No statistical analyses for this end point

Secondary: Bilirubin, Blood Urea Nitrogen (BUN), Uric Acid, Magnesium, Glucose, Cholesterol, Triglycerides, High sensitivity C-Reactive Protein (hsCRP), Inorganic phosphate, Corrected Calcium, and Creatinine: Mean Change from Baseline to Final Visit

| | |
|-----------------|--|
| End point title | Bilirubin, Blood Urea Nitrogen (BUN), Uric Acid, Magnesium, Glucose, Cholesterol, Triglycerides, High sensitivity C-Reactive Protein (hsCRP), Inorganic phosphate, Corrected Calcium, and Creatinine: Mean Change from Baseline to Final Visit |
|-----------------|--|

End point description:

n=subjects with evaluable Baseline and Post-baseline data for each parameter.

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

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

| End point values | Paricalcitol | | | |
|--------------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 ^[11] | | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Total bilirubin (n=11) | 0.032 (± 0.3165) | | | |
| Direct Bilirubin (n=11) | 0.013 (± 0.0785) | | | |
| Indirect Bilirubin (n=9) | 0.056 (± 0.3035) | | | |
| BUN (n=11) | 1.33 (± 11.614) | | | |
| Uric Acid (n=11) | 0.31 (± 1.245) | | | |
| Magnesium (n=11) | 0.082 (± 0.3649) | | | |
| Glucose (n=11) | 4.36 (± 10.172) | | | |
| Cholesterol (n=11) | -16.4 (± 27.37) | | | |
| Triglycerides (n=11) | 9.2 (± 40.32) | | | |
| hsCRP (n=11) | 0.061 (± 0.1967) | | | |
| Inorganic phosphate (n=13) | 0.64 (± 1.188) | | | |
| Corrected Calcium (n=7) | 0.31 (± 0.421) | | | |
| Creatinine (n=11) | 0.48 (± 1.592) | | | |

Notes:

[11] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Alkaline phosphatase: Mean Change from Baseline to Final Visit

| | |
|-----------------|--|
| End point title | Alkaline phosphatase: Mean Change from Baseline to Final Visit |
|-----------------|--|

End point description:

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

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

| End point values | Paricalcitol | | | |
|--------------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 ^[12] | | | |
| Units: IU/L | | | | |
| arithmetic mean (standard deviation) | -61.8 (± 117.34) | | | |

Notes:

[12] - All subjects in the all-treated data set with evaluable data

Statistical analyses

No statistical analyses for this end point

Secondary: Sodium, Potassium, Chloride, Bicarbonate: Mean Change from Baseline to Final Visit

| | |
|-----------------|--|
| End point title | Sodium, Potassium, Chloride, Bicarbonate: Mean Change from Baseline to Final Visit |
|-----------------|--|

End point description:

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

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

| End point values | Paricalcitol | | | |
|--------------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 ^[13] | | | |
| Units: mEq/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| Sodium | -0.5 (± 2.02) | | | |
| Potassium | 0.25 (± 0.746) | | | |
| Chloride | 0.5 (± 3.21) | | | |
| Bicarbonate | -0.45 (± 3.446) | | | |

Notes:

[13] - All subjects in the all-treated data set with evaluable data

Statistical analyses

No statistical analyses for this end point

Secondary: Total Protein and Albumin: Mean Change from Baseline to Final Visit

| | |
|------------------------|--|
| End point title | Total Protein and Albumin: Mean Change from Baseline to Final Visit |
| End point description: | n=subjects with evaluable Baseline and Post-baseline data for each parameter. |
| End point type | Secondary |
| End point timeframe: | Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12) |

| End point values | Paricalcitol | | | |
|--------------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 13 ^[14] | | | |
| Units: g/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Total protein (n=11) | 0.15 (± 0.43) | | | |
| Albumin (n=13) | 0.04 (± 0.325) | | | |

Notes:

[14] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Fibroblast Growth Factor-23 (FGF-23), 1,25-Hydroxy Vitamin D, 25-Hydroxy Vitamin D, and Intact Parathyroid Hormone (iPTH): Mean Change from Baseline to Final Visit

| | |
|------------------------|---|
| End point title | Fibroblast Growth Factor-23 (FGF-23), 1,25-Hydroxy Vitamin D, 25-Hydroxy Vitamin D, and Intact Parathyroid Hormone (iPTH): Mean Change from Baseline to Final Visit |
| End point description: | n=subjects with evaluable Baseline and Post-baseline data for each parameter. |
| End point type | Secondary |

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

| | | | | |
|--------------------------------------|--------------------|--|--|--|
| End point values | Paricalcitol | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 13 ^[15] | | | |
| Units: pg/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| FGF-23 (n=10) | 1990.7 (± 3317.79) | | | |
| 1,25-Hydroxy Vitamin D (n=11) | 15.65 (± 29.296) | | | |
| 25-Hydroxy Vitamin D (n=11) | 5.8 (± 10.38) | | | |
| iPTH (n=13) | -437.5 (± 491.83) | | | |

Notes:

[15] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Osteocalcin: Mean Change from Baseline to Final Visit

| | |
|------------------------|---|
| End point title | Osteocalcin: Mean Change from Baseline to Final Visit |
| End point description: | |

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

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

| | | | | |
|--------------------------------------|--------------------|--|--|--|
| End point values | Paricalcitol | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 10 ^[16] | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | 117.21 (± 223.075) | | | |

Notes:

[16] - All subjects in the all-treated data set with evaluable data

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adverse Events

| | |
|-----------------|--|
| End point title | Number of Subjects With Adverse Events |
|-----------------|--|

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. The investigator assessed the relationship of each event to the use of study drug as either probably related, possibly related, probably not related or not related. A serious adverse event (SAE) is an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the subject and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment-emergent events (TEAEs/TESAEs) are defined as any event that began or worsened in severity after the first dose of study drug. For more details on adverse events please see the Adverse Event section.

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

End point timeframe:

From first dose of study drug until 30 days following last dose of study drug (up to 16 weeks).

| End point values | Paricalcitol | | | |
|-----------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 13 ^[17] | | | |
| Units: subjects | | | | |
| Any TEAE | 11 | | | |
| TESAE | 2 | | | |

Notes:

[17] - All-treated data set

Statistical analyses

No statistical analyses for this end point

**Secondary: Number of Subjects with Potentially Clinically Significant
Electrocardiogram (ECG) Findings**

| | |
|-----------------|---|
| End point title | Number of Subjects with Potentially Clinically Significant Electrocardiogram (ECG) Findings |
|-----------------|---|

End point description:

12-lead ECGs were recorded after the subject had been in the supine position for at least 5 minutes. The number of subjects with potentially clinically significant ECG findings, as determined by the investigator, is presented.

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

End point timeframe:

Baseline (Day 1) to Final Visit (up to Week 12)

| End point values | Paricalcitol | | | |
|-----------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 13 ^[18] | | | |
| Units: subjects | 0 | | | |

Notes:

[18] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP): Mean Change from Baseline to Final Visit

| | |
|-----------------|--|
| End point title | Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP): Mean Change from Baseline to Final Visit |
|-----------------|--|

End point description:

Blood pressure was measured after the subject had been sitting for at least 3 minutes.

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

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

| End point values | Paricalcitol | | | |
|--------------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 13 ^[19] | | | |
| Units: mm Hg | | | | |
| arithmetic mean (standard deviation) | | | | |
| SBP | 7.5 (± 15.66) | | | |
| DBP | 3.7 (± 12.98) | | | |

Notes:

[19] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Heart Rate: Mean Change from Baseline to Final Visit

| | |
|-----------------|--|
| End point title | Heart Rate: Mean Change from Baseline to Final Visit |
|-----------------|--|

End point description:

Heart rate was measured after the subject had been sitting for at least 3 minutes.

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

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

| End point values | Paricalcitol | | | |
|--------------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 13 ^[20] | | | |
| Units: bpm | | | | |
| arithmetic mean (standard deviation) | 1.8 (± 17.43) | | | |

Notes:

[20] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Oral Body Temperature: Mean Change from Baseline to Final Visit

| | |
|-----------------|---|
| End point title | Oral Body Temperature: Mean Change from Baseline to Final Visit |
|-----------------|---|

End point description:

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

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

| End point values | Paricalcitol | | | |
|--------------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 13 ^[21] | | | |
| Units: degrees Celsius | | | | |
| arithmetic mean (standard deviation) | 0.03 (± 0.338) | | | |

Notes:

[21] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Potentially Clinically Significant Physical Examination Findings

| | |
|-----------------|--|
| End point title | Number of Subjects with Potentially Clinically Significant Physical Examination Findings |
|-----------------|--|

End point description:

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

End point timeframe:

Baseline (Day 1) and Final Visit (up to Week 12)

| End point values | Paricalcitol | | | |
|-----------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 13 ^[22] | | | |
| Units: subjects | 0 | | | |

Notes:

[22] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events were collected from first dose of study drug until 30 days following last dose of study drug (up to 16 weeks); serious adverse events were collected from the time when informed consent was obtained (up to 28 weeks).

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Paricalcitol |
|-----------------------|--------------|

Reporting group description:

Open-label paricalcitol (maximum dose of 16 µg), 3 times weekly (no more frequently than every other day) for 12 weeks.

| Serious adverse events | Paricalcitol | | |
|---|-----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Peritoneal dialysis complication | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Fluid overload | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Paricalcitol | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 10 / 13 (76.92%) | | |

| | | | |
|---|----------------------|--|--|
| Investigations Blood calcium increased subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |
| Haemoglobin decreased subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |
| Injury, poisoning and procedural complications Arteriovenous fistula site complication subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |
| Procedural pain subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |
| Procedural vomiting subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |
| General disorders and administration site conditions Influenza like illness subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |
| Pyrexia subjects affected / exposed occurrences (all) | 2 / 13 (15.38%) 2 | | |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |

| | | | |
|--|----------------------|--|--|
| Abdominal pain upper subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |
| Nausea subjects affected / exposed occurrences (all) | 2 / 13 (15.38%) 3 | | |
| Vomiting subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 2 / 13 (15.38%) 2 | | |
| Throat irritation subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |
| Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |
| Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |
| Metabolism and nutrition disorders | | | |

| | | | |
|--|---------------------|--|--|
| Hyperphosphataemia subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |
|--|---------------------|--|--|

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 24 May 2011 | The purpose of the amendment was to revise the definition of full immunosuppressant therapy, so otherwise eligible transplant patients were not excluded. |
| 21 August 2012 | The purpose of the amendment was to add a maximum iPTH value for entry into the Washout Period and increased the upper limit for corrected calcium for entry into the Dosing Period. In addition, the fasting requirement for blood draws was removed at all points in the study at the request of the investigators. |
| 29 August 2012 | The purpose of the amendment was to clarify that positive drug test results, due to controlled drugs prescribed for a medical need, were not exclusionary |
| 19 June 2013 | The purpose of the amendment was to revise the number of study sites to accommodate additional sites outside of the United States and add equivalent values in the units mmol/L for current calcium and phosphorus in the units mg/dL to comply with local standards. |
| 31 October 2013 | The purpose of the amendment was to modify the protocol so that subjects on hemodialysis could be included in the study. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The sample size of the study was limited to 13 subjects and there was no comparator group, so the study was not designed to analyze efficacy.

Notes: