Clinical trial results:
Efficacy and safety of paricalcitol in the reduction of secondary hyperparathyroidism after renal transplantation.

Summary

EudraCT number	2013-001326-25
Trial protocol	ES
Global end of trial date	09 September 2016

Results information

Result version number	v1 (current)
This version publication date	26 January 2020
First version publication date	26 January 2020

Trial information

Trial identification

Sponsor protocol code	ACA-SPAI-11-24

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01939977
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fundación SENEFRO
Sponsor organisation address	Calle Calvo Sotelo, 19 3ª planta, Santander, Spain, 39002
Public contact	Josep M Cruzado, Hospital Universitari de Bellvitge, 34 932607602, jmcruzado@bellvitgehospital.cat
Scientific contact	Josep M Cruzado, Hospital Universitari de Bellvitge, 34 932607602, jmcruzado@bellvitgehospital.cat

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	09 September 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 September 2016
Global end of trial reached?	Yes
Global end of trial date	09 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the superiority of paricalcitol treatment at early renal post-transplantation (M6) in the control of iPTH compared to the use of vitamin D nutritional supplements (calcifediol) in patients with renal transplantation.

Protection of trial subjects:

The study was in compliance with ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy:

in both treatment groups, the patients received standard treatment for transplant patients, which should include immunosuppression with tacrolimus, mycophenolate mofetil or mycophenolic acid and steroids.

Evidence for comparator: -

Actual start date of recruitment	07 January 2014
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	Spain: 148
Worldwide total number of subjects	148
EEA total number of subjects	148

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)	93
From 65 to 84 years	55

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First randomization took place on 07/01/2014 and the last randomization took place on 27/02/2015. 148 patients were screened; 94 were randomized at 13 sites. 1 patient did not receive the study treatment.

Pre-assignment

Screening details:

Signed IC;Age>18 years;Candidates to an immediately renal transplantation from living or deceased donor;Significant grade of hyperparathyroidism;Preformed antibody panel<20%;Serum calcium (corrected by albumin) < 10 mg/dL 24 hour previous to the transplantation;Patients treated with immunosupresion (not treated with mTOR inhibitors)

Period 1

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

Blinding implementation details:

No blinding techniques are applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Paricalcitol

Arm description:

Paricalcitol oral, 1 µg/day (Zemplar®, Abbvie Inc. North Chicago, Illinois, USA), plus the standard treatment for a renal transplant recipient. The starting dose of paricalcitol was 1 µg/day, but this dose was adjusted based on the serum iPTH and Ca* levels

Arm type	Experimental
Investigational medicinal product name	Paricalcitol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The patients assigned to Group 1 of treatment received 1 µg/day of paricalcitol as of the first day they tolerate oral nutrition, within the first week post-transplant. The dose of paricalcitol was adjusted based on the levels of serum iPTH and calcium:
If after the first month (M1 Visit), the serum levels of iPTH exceed 100 pg/ml and serum calcium is less than or equal to 10 mg/dl, the dose of paricalcitol will be increased to 2 µg/day, with strict control of serum iPTH and calcium.
If the calcium levels exceed 10.3 mg/dL, and the iPTH is ≤ 110 pg/ml, the dose of paricalcitol will be reduced to 1 µg on alternate days (1 µg of paricalcitol every 48h).
If, on the other hand, with those levels of calcium the iPTH > 110 pg/ml, the patient will be considered to not be responding to the treatment and, therefore, will leave the treatment and complete the End-of Study Visit.
This adjustment will also apply at the M3 Visit if necessary.

Arm title	Calcifediol

Arm description:

Calcifediol oral (Hidroferol®, FAES FARMA, Spain), plus the standard treatment for a renal transplant recipient. The starting dose was 5 drops (20 µg or 1200 IU) and the maintenance dose was adjusted based on the 25(OH)D levels.

Arm type	Active comparator

Investigational medicinal product name	Calcifediol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The patients assigned to Calcifediol of treatment received 5 drops of calcifediol per day (20 µg or 1200 IU) as of the first day they tolerate oral nutrition, within the first week post-transplant. The dose of calcifediol was adjusted based on the 25(OH)D levels measured at visits M1 and M3. Therefore:
If, at the M1 Visit, the 25(OH)D levels are ≥ 30 ng/ml, the patients will continue receiving 5 drops per day of oral calcifediol until the end of the study. If, at the M1 Visit, the 25(OH)D levels are < 30 ng/ml, the patients switched to receive 7 drops per day of calcifediol until the M3 Visit. If, at the M3 Visit, the 25(OH)D levels are ≥ 30 ng/ml, the patients switched to receive 5 drops per day of calcifediol until the end of the study. If, at the M3 Visit, the 25(OH)D levels continue to be < 30 ng/ml, the patients continued receiving 7 drops per day of calcifediol until the end of the study.

Number of subjects in period 1[1]	Paricalcitol	Calcifediol
Started	46	47
Completed	37	41
Not completed	9	6
Physician decision	1	1
Consent withdrawn by subject	-	2
Adverse event, non-fatal	4	3
Lack of efficacy	3	-
Protocol deviation	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 54 patients were failure of screening and 1 patient was not treated.

Baseline characteristics

Reporting groups	
Reporting group title	Paricalcitol
Reporting group description:	
Paricalcitol oral, 1 µg/day (Zemplar®, Abbvie Inc. North Chicago, Illinois, USA), plus the standard treatment for a renal transplant recipient. The starting dose of paricalcitol was 1 µg/day, but this dose was adjusted based on the serum iPTH and Ca* levels	
Reporting group title	Calcifediol
Reporting group description:	
Calcifediol oral (Hidroferol®, FAES FARMA, Spain), plus the standard treatment for a renal transplant recipient. The starting dose was 5 drops (20 µg or 1200 IU) and the maintenance dose was adjusted based on the 25(OH)D levels.	

Reporting group values	Paricalcitol	Calcifediol	Total
Number of subjects	46	47	93
Age categorical Units: Subjects			
Adults (18-64 years)	28	29	57
From 65-84 years	18	18	36
Age continuous Units: years			
median	62.5	56.0	
full range (min-max)	21 to 78	27 to 78	-
Gender categorical Units: Subjects			
Female	14	16	30
Male	32	31	63
Smoking Units: Subjects			
Non smoker	20	25	45
Former smoker	15	14	29
Smoker	11	8	19
Alcohol intake Units: Subjects			
Abstemious	38	37	75
Occasional	8	7	15
Regular	0	3	3
First renal transplant Units: Subjects			
Yes	43	44	87
No	3	3	6
Type of transplant Units: Subjects			
Living donor	9	11	20
Deceased donor	37	36	73
Donor gender Units: Subjects			
Male	20	23	43
Female	25	23	48

Unknown	1	1	2

Donor age			
Units: years			
median	64	60	
full range (min-max)	21 to 85	11 to 80	-

End points

End points reporting groups

Reporting group title	Paricalcitol
Reporting group description:	
Paricalcitol oral, 1 µg/day (Zemplar®, Abbvie Inc. North Chicago, Illinois, USA), plus the standard treatment for a renal transplant recipient. The starting dose of paricalcitol was 1 µg/day, but this dose was adjusted based on the serum iPTH and Ca* levels	
Reporting group title	Calcifediol
Reporting group description:	
Calcifediol oral (Hidroferol®, FAES FARMA, Spain), plus the standard treatment for a renal transplant recipient. The starting dose was 5 drops (20 µg or 1200 IU) and the maintenance dose was adjusted based on the 25(OH)D levels.	

Primary: iPTH serum concentration

End point title	iPTH serum concentration
End point description:	
Percentage of patients with iPTH serum concentration > 110 pg/ml	
End point type	Primary
End point timeframe:	
At six months post-transplantation after starting the study treatment in the 7 days post-transplantation.	

End point values	Paricalcitol	Calcifediol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41[1]	43[2]		
Units: subjects				
iPTH>110 pg/ml	9	16		
iPTH<=110 pg/ml	32	27		

Notes:

[1] - 5 missing data

[2] - 4 missing data

Statistical analyses

Statistical analysis title	Differences between groups
Comparison groups	Paricalcitol v Calcifediol
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1263
Method	Chi-squared

Secondary: Change in serum iPTH concentration

End point title	Change in serum iPTH concentration

End point description:

End point type	Secondary

End point timeframe:

At 6 months post-transplantation and 6 months of treatment in each study group

End point values	Paricalcitol	Calcifediol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	43		
Units: pg/ml				
arithmetic mean (confidence interval 95%)	-275.1 (-318.4 to -231.8)	-212.6 (-249.8 to -175.4)		

Statistical analyses

Statistical analysis title	Differences between groups
Comparison groups	Paricalcitol v Calcifediol
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0174
Method	ANOVA

Secondary: iPTH≥30% reduction

End point title	iPTH≥30% reduction

End point description:

Percentage of patients with at least iPTH ≥ 30% reduction with respect to baseline, throughout the study

End point type	Secondary

End point timeframe:

At six months post-transplantation after starting the study treatment in the 7 days post-transplantation

End point values	Paricalcitol	Calcifediol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	47		
Units: subjects				
iPTH>=30% reduction	43	46		
iPTH<30% reduction	3	1		

Statistical analyses

Statistical analysis title	Differences between groups
Comparison groups	Paricalcitol v Calcifediol
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3613
Method	Fisher exact

Secondary: iPTH levels between 70-110 pg/ml	
End point title	iPTH levels between 70-110 pg/ml
End point description:	
End point type	Secondary
End point timeframe:	
At six months post-transplantation after starting the study treatment in the 7 days post-transplantation	

End point values	Paricalcitol	Calcifediol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	43		
Units: subjects				
iPTH<70 pg/ml	26	16		
iPTH entre 70-110 pg/ml	6	11		
iPTH>=110 pg/ml	9	16		

Statistical analyses

Statistical analysis title	Differences between groups
Comparison groups	Calcifediol v Paricalcitol
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0559
Method	Chi-squared

Secondary: Presence of calcifications

End point title	Presence of calcifications
End point description:	
Percentage of patients with presence of calcifications on protocol renal biopsies at 6 months after treatment in each study group	
End point type	Secondary
End point timeframe:	
At 6 months after treatment	

End point values	Paricalcitol	Calcifediol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	19		
Units: subjects				
Yes	1	0		
No	16	19		

Statistical analyses

Statistical analysis title	Differences between groups
Comparison groups	Paricalcitol v Calcifediol
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4722
Method	Fisher exact

Secondary: Combined event

End point title	Combined event
End point description:	
Incidence of at least of the following events: acute rejection, biopsy-proven acute rejection (BPAR) and/or subclinical rejection (ScR) and/or chronic damage (IFTA).	
End point type	Secondary
End point timeframe:	
During the study	

End point values	Paricalcitol	Calcifediol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	21		
Units: subjects	14	6		

Statistical analyses

Statistical analysis title	Differences between groups
Comparison groups	Calcifediol v Paricalcitol
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0814
Method	Chi-squared

Secondary: Osteocalcin

End point title	Osteocalcin

End point description:

End point type	Secondary

End point timeframe:

At 6 months post-transplantation and of treatment in each study group

End point values	Paricalcitol	Calcifediol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	41		
Units: ng/mL				
arithmetic mean (confidence interval 95%)	-7.13 (-10.0 to -4.2)	-7.81 (-10.5 to -5.1)		

Statistical analyses

Statistical analysis title	Differences between groups
Comparison groups	Paricalcitol v Calcifediol
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.391
Method	ANOVA

Secondary: Alkaline phosphatase

End point title	Alkaline phosphatase

End point description:

End point type	Secondary

End point timeframe:

At 6 months post-transplantation

End point values	Paricalcitol	Calcifediol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	42		
Units: µg/L				
arithmetic mean (confidence interval 95%)	-1.90 (-5.1 to 1.3)	-2.68 (-5.1 to -0.3)		

Statistical analyses

Statistical analysis title	Differences between groups
Comparison groups	Paricalcitol v Calcifediol
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1811
Method	ANOVA

Secondary: FGF-23

End point title	FGF-23

End point description:

End point type	Secondary

End point timeframe:

at 6 months post-transplantation

End point values	Paricalcitol	Calcifediol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	42		
Units: pg/ml				
arithmetic mean (confidence interval 95%)	-633.5 (-3200 to 1933)	-1712 (-2944 to -481)		

Statistical analyses

Statistical analysis title	Differences between groups
Comparison groups	Paricalcitol v Calcifediol
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2494
Method	ANOVA

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Overall period	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Paricalcitol
Reporting group description:	
Paricalcitol oral, 1 µg/day (Zemplar®, Abbvie Inc. North Chicago, Illinois, USA), plus the standard treatment for a renal transplant recipient. The starting dose of paricalcitol was 1 µg/day, but this dose was adjusted based on the serum iPTH and Ca* levels	
Reporting group title	Calcifediol
Reporting group description:	
Calcifediol oral (Hidroferol®, FAES FARMA, Spain), plus the standard treatment for a renal transplant recipient. The starting dose was 5 drops (20 µg or 1200 IU) and the maintenance dose was adjusted based on the 25(OH)D levels.	

Serious adverse events	Paricalcitol	Calcifediol	
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 46 (52.17%)	20 / 47 (42.55%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinoma transitional cell			
subjects affected / exposed	0 / 46 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 46 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocele			
subjects affected / exposed	1 / 46 (2.17%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Surgical and medical procedures			
Removal of renal transplant			
subjects affected / exposed	0 / 46 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocele marsupialisation			
subjects affected / exposed	1 / 46 (2.17%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Administration site extravasation			
subjects affected / exposed	0 / 46 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 46 (4.35%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Transplant rejection			
subjects affected / exposed	1 / 46 (2.17%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 46 (2.17%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute pulmonary oedema			
subjects affected / exposed	1 / 46 (2.17%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism lung			

subjects affected / exposed	0 / 46 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Pseudomonas test positive			
subjects affected / exposed	0 / 46 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Cicatrix skin			
subjects affected / exposed	1 / 46 (2.17%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perinephric collection			
subjects affected / exposed	0 / 46 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 46 (2.17%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Depressed level of consciousness			
subjects affected / exposed	1 / 46 (2.17%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy			
subjects affected / exposed	0 / 46 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Thrombotic microangiopathy			

subjects affected / exposed	1 / 46 (2.17%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 46 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 46 (2.17%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal haemorrhage			
subjects affected / exposed	0 / 46 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	1 / 46 (2.17%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal disorder			
subjects affected / exposed	7 / 46 (15.22%)	3 / 47 (6.38%)	
occurrences causally related to treatment / all	0 / 8	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dilatation ureteral			
subjects affected / exposed	1 / 46 (2.17%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 46 (0.00%)	2 / 47 (4.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Acute kidney injury			
subjects affected / exposed	0 / 46 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proteinuria			
subjects affected / exposed	0 / 46 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cytomegalovirus colitis			
subjects affected / exposed	0 / 46 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	5 / 46 (10.87%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BK virus infection			
subjects affected / exposed	0 / 46 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	2 / 46 (4.35%)	2 / 47 (4.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 46 (2.17%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	1 / 46 (2.17%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 46 (2.17%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 46 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Paricalcitol	Calcifediol	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 46 (89.13%)	38 / 47 (80.85%)	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 46 (15.22%)	1 / 47 (2.13%)	
occurrences (all)	7	1	
Leucocitosis			
subjects affected / exposed	5 / 46 (10.87%)	3 / 47 (6.38%)	
occurrences (all)	5	3	
General disorders and administration site conditions			
Oedema			
subjects affected / exposed	3 / 46 (6.52%)	2 / 47 (4.26%)	
occurrences (all)	5	2	
Oedema peripheral			
subjects affected / exposed	3 / 46 (6.52%)	4 / 47 (8.51%)	
occurrences (all)	4	5	
Pyrexia			
subjects affected / exposed	4 / 46 (8.70%)	2 / 47 (4.26%)	
occurrences (all)	5	2	
Immune system disorders			

Transplant rejection			
subjects affected / exposed	3 / 46 (6.52%)	1 / 47 (2.13%)	
occurrences (all)	3	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	7 / 46 (15.22%)	4 / 47 (8.51%)	
occurrences (all)	7	4	
Constipation			
subjects affected / exposed	3 / 46 (6.52%)	1 / 47 (2.13%)	
occurrences (all)	3	1	
Vomiting			
subjects affected / exposed	1 / 46 (2.17%)	3 / 47 (6.38%)	
occurrences (all)	1	3	
Renal and urinary disorders			
Renal disorder			
subjects affected / exposed	9 / 46 (19.57%)	5 / 47 (10.64%)	
occurrences (all)	11	6	
Haematuria			
subjects affected / exposed	2 / 46 (4.35%)	3 / 47 (6.38%)	
occurrences (all)	3	4	
Proteinuria			
subjects affected / exposed	0 / 46 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	4	
Renal tubular necrosis			
subjects affected / exposed	3 / 46 (6.52%)	1 / 47 (2.13%)	
occurrences (all)	3	1	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	16 / 46 (34.78%)	6 / 47 (12.77%)	
occurrences (all)	22	7	
Cytomegalovirus infection			
subjects affected / exposed	4 / 46 (8.70%)	4 / 47 (8.51%)	
occurrences (all)	4	4	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	3 / 46 (6.52%)	4 / 47 (8.51%)	
occurrences (all)	3	4	

Hyperglycaemia subjects affected / exposed occurrences (all)	3 / 46 (6.52%) 3	0 / 47 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 May 2014	- Regarding the modification of inclusion criteria # 3: Studies published last year with a similar objective on the effect of paricalcitol on PTH in transplant patients (Amer et al. Am J Trasplant 2013; Pérez et al. Eur J Pharmacol 2013) measured the effect of the drug on patients with any grade of HPTS (PTH> 65 pg / mL and medians around 100 pg / mL, respectively). In addition, the SEN guidelines (current 2011) recommend the treatment of PTH of the renal patient from plasma values above 70 pg / mL (filtered below 60 mL / min, stage 3) and above 110 pg / mL (filtered below 30 mL / min, stage 4) we consider it sufficient for the patient to have PTH levels above 110 pg / mL to be included in the study. In this way, the degree of HPTS to be treated is extended, being more similar to the usual clinical practice. - The number of tubes to be extracted has been clarified, since finally a smaller blood sample was needed to perform the corresponding analyzes

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported