

**Clinical trial results:****A PROSPECTIVE, RANDOMIZED, CROSS-OVER, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO ASSESS THE ANTIPROTEINURIC EFFECT OF SELECTIVE VITAMIN D RECEPTOR ACTIVATION BY PARICALCITOL IN TYPE 2 DIABETES PATIENTS ON LOW OR HIGH SODIUM DIET AND STABLE RAS INHIBITOR THERAPY****Summary**

EudraCT number	2011-001713-14
Trial protocol	IT
Global end of trial date	29 May 2015

Results information

Result version number	v1 (current)
This version publication date	02 June 2019
First version publication date	02 June 2019
Summary attachment (see zip file)	Paper Lancet Diabetes Endocrinol 2017 (Proceed_Paper_2017.pdf) Supplementary appendix (Proceed supplementary.pdf)

Trial information**Trial identification**

Sponsor protocol code	PROCEED
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01393808
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Istituto di Ricerche Farmacologiche Mario Negri IRCCS
Sponsor organisation address	via G. La Masa 19, Milano MI, Italy, 20156
Public contact	Laboratorio attività regolatorie relative agli studi clinici, Centro di Ricerche Cliniche per le Malattie Rare Aldo e Cele Daccò, 0039 035 453531, paola.boccardo@marionegri.it
Scientific contact	Laboratorio attività regolatorie relative agli studi clinici, Centro di Ricerche Cliniche per le Malattie Rare Aldo e Cele Daccò, 0039 035 453531, paola.boccardo@marionegri.it

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 November 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 May 2015
Global end of trial reached?	Yes
Global end of trial date	29 May 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The broad aim of this study was to evaluate the interaction between paricalcitol therapy and sodium intake in type 2 diabetes patients with proteinuric kidney disease on stable background RAS inhibitor therapy.

The primary aim was to compare changes in Urinary Albumin Excretion (UAE) rate achieved by one month paricalcitol therapy vs placebo in patients on stable Renin-Angiotensin System (RAS) inhibitor therapy on high (>200 mEq/day) or low (<100 mEq/day) sodium intake.

Protection of trial subjects:

This study was conducted in conformance with Declaration of Helsinki, Good Clinical Practice standards and applicable country regulations regarding ethical committee review, informed consent, protection of human subjects participating in biomedical research and privacy.

We assessed by monitoring of vital signs, physical examination, (BP and heart rate), laboratory tests, adverse event data and documentation of additional medication use, assessed at baseline and at the end of each monthly visit.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 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	Italy: 115
Worldwide total number of subjects	115
EEA total number of subjects	115

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	56
From 65 to 84 years	59
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All participating centers in Italy were activated between September and October 2011. The recruitment started on October 13, 2011 and concluded on December 18, 2014.

Pre-assignment

Screening details:

195 subjects were screened for inclusion in the study. 115 subjects were randomized. Of those not randomised, 55 did not meet inclusion criteria, 1 was lost to follow up, 22 declined to participate and 2 were excluded for concomitant diseases.

Period 1

Period 1 title	Treatment Period 1 (1 month)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A - Stratum Low Sodium Diet Paricalcitol

Arm description:

Participants received Paricalcitol 1 microgram tablets twice daily for 1 month during Treatment period 1 and received Placebo tablets twice daily for 1 month during Treatment period 3.

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

Dosage and administration details:

Paricalcitol 1 microgram tablets orally twice daily for 1 month.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo tablets orally twice daily for 1 month.

Arm title	Group B - Stratum Low Sodium Diet Placebo
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Arm description:

Participants received placebo tablets twice daily for 1 month during Treatment period 1 and received Paricalcitol 1 micrograms tablets twice daily for 1 month during Treatment period 3. There is one-month wash-out period between Treatment periods 1 and 3

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

Dosage and administration details:	
Placebo tablets orally twice daily for 1 month.	
Investigational medicinal product name	Paricalcitol
Investigational medicinal product code	
Other name	Zemplar
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Paricalcitol 1 microgram tablets orally twice daily for 1 month.	
Arm title	Group C - Stratum High Sodium Diet Paricalcitol
Arm description:	
Participants received Paricalcitol 1 microgram tablets twice daily for 1 month during treatment period 1 and received Placebo twice daily for 1 month during treatment period 3.	
Arm type	Experimental
Investigational medicinal product name	Paricalcitol
Investigational medicinal product code	
Other name	Zemplar
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Paricalcitol 1 microgram tablets orally twice daily for 1 month.	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Placebo tablets orally twice daily for 1 month.	
Arm title	Group D - Stratum High Sodium Diet Placebo
Arm description:	
Participants received placebo tablets twice daily for 1 month during treatment period 1 and received Paricalcitol 1 microgram tablets twice daily for 1 month during treatment period 3.	
Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Placebo tablets orally twice daily for 1 month.	
Investigational medicinal product name	Paricalcitol
Investigational medicinal product code	
Other name	Zemplar
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Paricalcitol 1 microgram tablets orally twice daily for 1 month.	

Number of subjects in period 1	Group A - Stratum Low Sodium Diet Paricalcitol	Group B - Stratum Low Sodium Diet Placebo	Group C - Stratum High Sodium Diet Paricalcitol
Started	28	29	29
Completed	28	28	28
Not completed	0	1	1
Consent withdrawn by subject	-	1	1
Protocol deviation	-	-	-

Number of subjects in period 1	Group D - Stratum High Sodium Diet Placebo
Started	29
Completed	27
Not completed	2
Consent withdrawn by subject	1
Protocol deviation	1

Period 2

Period 2 title	Treatment period 2 (1 month - washout)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	No
Arm title	Group A - Stratum Low Sodium Diet placebo

Arm description:

Participants received Placebo tablets orally twice daily for 1 month (for patients that were on Paricalcitol during previous period)

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo tablets orally twice daily for 1 month.

Arm title	Group B - Stratum Low Sodium Diet placebo
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Arm description:

Participants received Placebo tablets orally twice daily for 1 month (for patients that were on Placebo during previous period)

Arm type	Placebo
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Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo tablets orally twice daily for 1 month.

Arm title	Group C - Stratum High Sodium Diet placebo
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Arm description:

Participants received Placebo tablets (for patients that were on Paricalcitol during previous period)

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

Dosage and administration details:

Placebo tablets orally twice daily for 1 month.

Arm title	Group D - Stratum High Sodium Diet placebo
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Arm description:

Participants received Placebo tablets twice daily for 1 month (for patients that were on Placebo during previous period)

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo tablets orally twice daily for 1 month.

Number of subjects in period 2	Group A - Stratum Low Sodium Diet placebo	Group B - Stratum Low Sodium Diet placebo	Group C - Stratum High Sodium Diet placebo
Started	28	28	28
Completed	27	28	28
Not completed	1	0	0
Consent withdrawn by subject	1	-	-

Number of subjects in period 2	Group D - Stratum High Sodium Diet placebo
Started	27
Completed	27
Not completed	0
Consent withdrawn by subject	-

Period 3	
Period 3 title	Treatment period 3 (1 month)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor
Arms	
Are arms mutually exclusive?	Yes
Arm title	Group A - Stratum Low Sodium Diet Placebo
Arm description:	
Participants received placebo tablets twice daily for 1 month during treatment period 3 and received Paricalcitol 1 microgram tablets twice daily for 1 month during treatment period 1.	
Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Placebo tablets orally twice daily for 1 month.	
Investigational medicinal product name	Paricalcitol
Investigational medicinal product code	
Other name	Zemplar
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Paricalcitol 1 microgram tablets orally twice daily for 1 month.	
Arm title	Group B - Stratum Low Sodium Diet Paricalcitol
Arm description:	
Participants received Paricalcitol 1 microgram tablets twice daily for 1 month during treatment period 3 and received placebo tablets twice daily for 1 month during treatment period 1.	
Arm type	Experimental
Investigational medicinal product name	Paricalcitol
Investigational medicinal product code	
Other name	Zemplar
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Paricalcitol 1 microgram tablets orally twice daily for 1 month.	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Placebo tablets orally twice daily for 1 month.	
Arm title	Group C - Stratum High Sodium Diet Placebo

Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Paricalcitol
Investigational medicinal product code	
Other name	Zemplar
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Paricalcitol 1 microgram tablets orally twice daily for 1 month.	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Zemplar
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Paricalcitol 1 microgram tablets orally twice daily for 1 month.	
Arm title	Group D - Stratum Low Sodium Diet Paricalcitol

Arm description:

Participants received Paricalcitol 1 microgram tablets twice daily for 1 month during treatment period 3 and received Placebo tablets twice daily for 1 month during treatment period 1.

Arm type	Experimental
Investigational medicinal product name	Paricalcitol
Investigational medicinal product code	
Other name	Zemplar
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Paricalcitol 1 microgram tablets orally twice daily for 1 month.	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Zemplar
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Paricalcitol 1 microgram tablets orally twice daily for 1 month.

Number of subjects in period 3	Group A - Stratum Low Sodium Diet Placebo	Group B - Stratum Low Sodium Diet Paricalcitol	Group C - Stratum High Sodium Diet Placebo
Started	27	28	28
Completed	27	26	28
Not completed	0	2	0
Lost to follow-up	-	2	-

Number of subjects in period 3	Group D - Stratum Low Sodium Diet Paricalcitol
Started	27
Completed	27
Not completed	0

Lost to follow-up	-
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Period 4

Period 4 title	Stratification and Treatment
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Low Sodium Diet

Arm description:

Participants stratified for Low sodium diet (Paricalcitol and Placebo)

Arm type	Diet
No investigational medicinal product assigned in this arm	

Arm title	High Sodium Diet
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Arm description:

Participants stratified for High sodium diet (Paricalcitol and Placebo)

Arm type	Diet
No investigational medicinal product assigned in this arm	

Arm title	Paricalcitol in High Sodium Diet
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Arm description:

Participants stratified for High sodium diet who took in Paricalcitol regardless of the IMP randomization sequence (Paricalcitol/Placebo or Placebo/Paricalcitol)

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

Dosage and administration details:

Paricalcitol 1 microgram tablets orally twice daily for 1 month.

Arm title	Placebo in High Sodium Diet
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Arm description:

Participants stratified for High sodium diet who took in Placebo regardless of the IMP randomization sequence (Paricalcitol/Placebo or Placebo/Paricalcitol)

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo tablets orally twice daily for 1 month.

Arm title	Paricalcitol in Low Sodium diet
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Arm description:

Participants stratified for Low sodium diet who took in Paricalcitol regardless of the IMP randomization sequence (Paricalcitol/Placebo or Placebo/Paricalcitol)

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

Dosage and administration details:

Paricalcitol 1 microgram tablets orally twice daily for 1 month.

Arm title	Placebo in Low Sodium Diet
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Arm description:

Participants stratified for Low sodium diet who took in Placebo regardless of the IMP randomization sequence (Paricalcitol/Placebo or Placebo/Paricalcitol)

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo tablets orally twice daily for 1 month.

Number of subjects in period 4	Low Sodium Diet	High Sodium Diet	Paricalcitol in High Sodium Diet
Started	57	58	58
Completed	53	55	55
Not completed	4	3	3
Consent withdrawn by subject	2	2	2
Lost to follow-up	2	-	-
Protocol deviation	-	1	1

Number of subjects in period 4	Placebo in High Sodium Diet	Paricalcitol in Low Sodium diet	Placebo in Low Sodium Diet
Started	58	57	57
Completed	55	53	53
Not completed	3	4	4
Consent withdrawn by subject	2	2	2
Lost to follow-up	-	2	2
Protocol deviation	1	-	-

Baseline characteristics

Reporting groups

Reporting group title	Group A - Stratum Low Sodium Diet Paricalcitol
Reporting group description: Participants received Paricalcitol 1 microgram tablets twice daily for 1 month during Treatment period 1 and received Placebo tablets twice daily for 1 month during Treatment period 3.	
Reporting group title	Group B - Stratum Low Sodium Diet Placebo
Reporting group description: Participants received placebo tablets twice daily for 1 month during Treatment period 1 and received Paricalcitol 1 micrograms tablets twice daily for 1 month during Treatment period 3. There is one-month wash-out period between Treatment periods 1 and 3	
Reporting group title	Group C - Stratum High Sodium Diet Paricalcitol
Reporting group description: Participants received Paricalcitol 1 microgram tablets twice daily for 1 month during treatment period 1 and received Placebo twice daily for 1 month during treatment period 3.	
Reporting group title	Group D - Stratum High Sodium Diet Placebo
Reporting group description: Participants received placebo tablets twice daily for 1 month during treatment period 1 and received Paricalcitol 1 microgram tablets twice daily for 1 month during treatment period 3.	

Reporting group values	Group A - Stratum Low Sodium Diet Paricalcitol	Group B - Stratum Low Sodium Diet Placebo	Group C - Stratum High Sodium Diet Paricalcitol
Number of subjects	28	29	29
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	11	16	14
From 65-84 years	17	13	15
85 years and over	0	0	0
age	0	0	0
Age continuous Units: years			
arithmetic mean	65.0	64.2	64.2
standard deviation	± 6.3	± 8.2	± 10.8
Gender categorical Units: Subjects			
Female	0	3	6
Male	28	26	23
Patients taking Losartan alone Units: Subjects			
Monotherapy	2	6	4
No monotherapy	26	23	25
Smoke			

Units: Subjects			
Never	6	3	4
Current	7	12	10
Former	15	14	15
Body Mass Index			
Units: kg/m ²			
arithmetic mean	31.2	31.4	29.1
standard deviation	± 3.5	± 5.0	± 4.0
Weight			
Units: kg			
arithmetic mean	90.7	91.5	81.1
standard deviation	± 13.7	± 16.7	± 14.6
Systolic Blood Pressure			
Units: mm HG			
arithmetic mean	147.6	148.2	146.3
standard deviation	± 12.0	± 14.1	± 11.4
Diastolic Blood Pressure			
Units: mm Hg			
arithmetic mean	81.1	79.0	79.8
standard deviation	± 5.4	± 7.0	± 5.9
Mean Blood Pressure			
Units: mm Hg			
arithmetic mean	102.9	102.5	101.6
standard deviation	± 6.8	± 7.8	± 6.5
Serum calcium			
Units: mg/dL			
arithmetic mean	9.1	9.1	9.3
standard deviation	± 0.3	± 0.4	± 0.3
Serum Phosphorus			
Units: mg/dL			
arithmetic mean	3.3	3.3	3.5
standard deviation	± 0.4	± 0.6	± 0.5
Serum iPTH			
Units: pg/mL			
arithmetic mean	50.0	50.0	42.1
standard deviation	± 22.4	± 20.0	± 22.1
Serum 25OH vit D			
Units: ng/mL			
arithmetic mean	12.25	12.1	10.6
standard deviation	± 5.7	± 6.4	± 4.6
Serum Glucose			
Units: mg/dL			
arithmetic mean	148.7	149.6	163.8
standard deviation	± 41.4	± 47.9	± 65.0
HbA1C			
Units: Percentual			
arithmetic mean	7.7	7.4	7.8
standard deviation	± 3.4	± 3.2	± 3.7
Serum potassium			
Units: meq/L			
arithmetic mean	4.0	4.2	4.2
standard deviation	± 0.5	± 0.6	± 0.6

Total cholesterol Units: mg/dL arithmetic mean standard deviation	166.9 ± 48.3	171.9 ± 32.7	174.7 ± 40.7
HDL cholesterol Units: mg/dL arithmetic mean standard deviation	42.5 ± 12.1	41 ± 9.6	47.5 ± 14.2
LDL cholesterol Units: mg/dL arithmetic mean standard deviation	94.7 ± 37.2	105.4 ± 32.0	107.2 ± 36.2
Triglycerides Units: mg/dL arithmetic mean standard deviation	177.7 ± 140.5	164.6 ± 71.1	134.8 ± 78.5
Hemoglobin Units: mg/dL arithmetic mean standard deviation	13.8 ± 1.4	13.7 ± 1.5	13.5 ± 1.5
24 h urinary calcium excretion Units: mg median inter-quartile range (Q1-Q3)	82.7 43.9 to 123.3	90.6 41.1 to 149.7	76.3 45.0 to 116.2
Glomerular Filtration Rate Units: mL/min/1.73m2 arithmetic mean standard deviation	87.33 ± 21.14	94.22 ± 33.08	81.51 ± 26.27
24 h urinary phosphorus excretion Units: mg median inter-quartile range (Q1-Q3)	617.7 542.7 to 828.5	763.1 546.0 to 986.2	634.3 429.2 to 860.8
24 h urinary albumin excretion Units: mg median inter-quartile range (Q1-Q3)	749 402 to 1493	724 449 to 1198	750 505 to 1338
24 h albumin-to-creatinine ratio Units: mg/g median inter-quartile range (Q1-Q3)	447.0 355.9 to 1070.9	548.5 254.1 to 693.9	604.3 421.8 to 806.9
Urinary Sodium Excretion Units: mEq/24h median inter-quartile range (Q1-Q3)	184.4 157.4 to 229.6	203.1 173.5 to 223.4	200.2 151.3 to 226.5
Reporting group values	Group D - Stratum High Sodium Diet Placebo	Total	
Number of subjects	29	115	
Age categorical Units: Subjects			
In utero	0	0	

Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	15	56	
From 65-84 years	14	59	
85 years and over	0	0	
age	0	0	
Age continuous			
Units: years			
arithmetic mean	64.1		
standard deviation	± 9.1	-	
Gender categorical			
Units: Subjects			
Female	4	13	
Male	25	102	
Patients taking Losartan alone			
Units: Subjects			
Monotherapy	7	19	
No monotherapy	22	96	
Smoke			
Units: Subjects			
Never	11	24	
Current	6	35	
Former	12	56	
Body Mass Index			
Units: kg/m2			
arithmetic mean	31.7		
standard deviation	± 6.1	-	
Weight			
Units: kg			
arithmetic mean	88.7		
standard deviation	± 18.8	-	
Systolic Blood Pressure			
Units: mm HG			
arithmetic mean	143.1		
standard deviation	± 12.6	-	
Diastolic Blood Pressure			
Units: mm Hg			
arithmetic mean	77.9		
standard deviation	± 5.2	-	
Mean Blood Pressure			
Units: mm Hg			
arithmetic mean	99.3		
standard deviation	± 6.4	-	
Serum calcium			
Units: mg/dL			
arithmetic mean	9.2		
standard deviation	± 0.3	-	

Serum Phosphorus Units: mg/dL arithmetic mean standard deviation	3.4 ± 0.5	-	
Serum iPTH Units: pg/mL arithmetic mean standard deviation	48.2 ± 23.2	-	
Serum 25OH vit D Units: ng/mL arithmetic mean standard deviation	12.8 ± 6.6	-	
Serum Glucose Units: mg/dL arithmetic mean standard deviation	151.3 ± 56.3	-	
HbA1C Units: Percentual arithmetic mean standard deviation	7.0 ± 3.4	-	
Serum potassium Units: meq/L arithmetic mean standard deviation	4.1 ± 0.4	-	
Total cholesterol Units: mg/dL arithmetic mean standard deviation	176.9 ± 34.4	-	
HDL cholesterol Units: mg/dL arithmetic mean standard deviation	43 ± 13.3	-	
LDL cholesterol Units: mg/dL arithmetic mean standard deviation	105.1 ± 24.4	-	
Triglycerides Units: mg/dL arithmetic mean standard deviation	178.5 ± 125.3	-	
Hemoglobin Units: mg/dL arithmetic mean standard deviation	13.1 ± 1.8	-	
24 h urinary calcium excretion Units: mg median inter-quartile range (Q1-Q3)	67.6 55.0 to 136.2	-	
Glomerular Filtration Rate Units: mL/min/1.73m2 arithmetic mean standard deviation	86.37 ± 34.51	-	

24 h urinary phosphorus excretion Units: mg median inter-quartile range (Q1-Q3)	779.3 539.1 to 914.5	-	
24 h urinary albumin excretion Units: mg median inter-quartile range (Q1-Q3)	658 389 to 1058	-	
24 h albumin-to-creatinine ratio Units: mg/g median inter-quartile range (Q1-Q3)	458.5 240.7 to 683.3	-	
Urinary Sodium Excretion Units: mEq/24h median inter-quartile range (Q1-Q3)	181.8 144.4 to 223.5	-	

End points

End points reporting groups

Reporting group title	Group A - Stratum Low Sodium Diet Paricalcitol
Reporting group description: Participants received Paricalcitol 1 microgram tablets twice daily for 1 month during Treatment period 1 and received Placebo tablets twice daily for 1 month during Treatment period 3.	
Reporting group title	Group B - Stratum Low Sodium Diet Placebo
Reporting group description: Participants received placebo tablets twice daily for 1 month during Treatment period 1 and received Paricalcitol 1 micrograms tablets twice daily for 1 month during Treatment period 3. There is one-month wash-out period between Treatment periods 1 and 3	
Reporting group title	Group C - Stratum High Sodium Diet Paricalcitol
Reporting group description: Participants received Paricalcitol 1 microgram tablets twice daily for 1 month during treatment period 1 and received Placebo twice daily for 1 month during treatment period 3.	
Reporting group title	Group D - Stratum High Sodium Diet Placebo
Reporting group description: Participants received placebo tablets twice daily for 1 month during treatment period 1 and received Paricalcitol 1 microgram tablets twice daily for 1 month during treatment period 3.	
Reporting group title	Group A - Stratum Low Sodium Diet placebo
Reporting group description: Participants received Placebo tablets orally twice daily for 1 month (for patients that were on Paricalcitol during previous period)	
Reporting group title	Group B - Stratum Low Sodium Diet placebo
Reporting group description: Participants received Placebo tablets orally twice daily for 1 month (for patients that were on Placebo during previous period)	
Reporting group title	Group C - Stratum High Sodium Diet placebo
Reporting group description: Participants received Placebo tablets (for patients that were on Paricalcitol during previous period)	
Reporting group title	Group D - Stratum High Sodium Diet placebo
Reporting group description: Participants received Placebo tablets twice daily for 1 month (for patients that were on Placebo during previous period)	
Reporting group title	Group A - Stratum Low Sodium Diet Placebo
Reporting group description: Participants received placebo tablets twice daily for 1 month during treatment period 3 and received Paricalcitol 1 microgram tablets twice daily for 1 month during treatment period 1.	
Reporting group title	Group B - Stratum Low Sodium Diet Paricalcitol
Reporting group description: Participants received Paricalcitol 1 microgram tablets twice daily for 1 month during treatment period 3 and received placebo tablets twice daily for 1 month during treatment period 1.	
Reporting group title	Group C - Stratum High Sodium Diet Placebo
Reporting group description: -	
Reporting group title	Group D - Stratum Low Sodium Diet Paricalcitol
Reporting group description: Participants received Paricalcitol 1 microgram tablets twice daily for 1 month during treatment period 3 and received Placebo tablets twice daily for 1 month during treatment period 1.	
Reporting group title	Low Sodium Diet
Reporting group description: Participants stratified for Low sodium diet (Paricalcitol and Placebo)	
Reporting group title	High Sodium Diet

Reporting group description:

Participants stratified for High sodium diet (Paricalcitol and Placebo)

Reporting group title	Paricalcitol in High Sodium Diet
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Reporting group description:

Participants stratified for High sodium diet who took in Paricalcitol regardless of the IMP randomization sequence (Paricalcitol/Placebo or Placebo/Paricalcitol)

Reporting group title	Placebo in High Sodium Diet
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Reporting group description:

Participants stratified for High sodium diet who took in Placebo regardless of the IMP randomization sequence (Paricalcitol/Placebo or Placebo/Paricalcitol)

Reporting group title	Paricalcitol in Low Sodium diet
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Reporting group description:

Participants stratified for Low sodium diet who took in Paricalcitol regardless of the IMP randomization sequence (Paricalcitol/Placebo or Placebo/Paricalcitol)

Reporting group title	Placebo in Low Sodium Diet
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Reporting group description:

Participants stratified for Low sodium diet who took in Placebo regardless of the IMP randomization sequence (Paricalcitol/Placebo or Placebo/Paricalcitol)

Primary: Changes in UAE rate between patients on paricalcitol and placebo on high (>200 mEq/day) or low (<100 mEq/day) sodium intake.

End point title	Changes in UAE rate between patients on paricalcitol and placebo on high (>200 mEq/day) or low (<100 mEq/day) sodium intake.
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End point description:

24 h urinary albumin excretion absolute change

End point type	Primary
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End point timeframe:

Baseline is at the start of treatment and after treatment is after the 1 month of Paricalcitol or Placebo treatment

End point values	Low Sodium Diet	High Sodium Diet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	55		
Units: mg/24h				
median (inter-quartile range (Q1-Q3))	-33.1 (-128.2 to 56.2)	-108.0 (-273.6 to -24.5)		

Statistical analyses

Statistical analysis title	Changes in UAE
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Statistical analysis description:

Changes in UAE between paricalcitol and placebo period, over sodium intake

Comparison groups	Low Sodium Diet v High Sodium Diet
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Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.09 ^[1]
Method	ANCOVA

Notes:

[1] - The report p-value is referred to overall patients changes in UAE between paricalcitol and placebo periods.

Changes in patients on High Sodium Diet reported a p-value of 0.09, while changes in patients on Low Sodium Diet reported a p-value of 0.55.

Post-hoc: Changes in UAE at the end of the treatment period 1 (1 month) as compared to baseline in patients on Stratum Low Sodium or High Sodium independently of treatment allocation to Placebo or Paricalcitol

End point title	Changes in UAE at the end of the treatment period 1 (1 month) as compared to baseline in patients on Stratum Low Sodium or High Sodium independently of treatment allocation to Placebo or Paricalcitol
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End point description:

End point type	Post-hoc
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End point timeframe:

Baseline to the end of first month of treatment.

End point values	Low Sodium Diet	High Sodium Diet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56 ^[2]	55 ^[3]		
Units: mg				
median (inter-quartile range (Q1-Q3))	-144 (-217.4 to -102.2)	-49 (-201.6 to 21.6)		

Notes:

[2] - 1 withdrew consent

[3] - 2 withdrew consent and 1 violated protocol

Statistical analyses

No statistical analyses for this end point

Post-hoc: Changes in UAE at the end of the washout period (1 month) as compared to baseline in patients on Stratum Low Sodium or High Sodium independently of treatment allocation to Placebo or Paricalcitol

End point title	Changes in UAE at the end of the washout period (1 month) as compared to baseline in patients on Stratum Low Sodium or High Sodium independently of treatment allocation to Placebo or Paricalcitol
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End point description:

End point type	Post-hoc
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End point timeframe:

Baseline to the second month of treatment.

End point values	Low Sodium Diet	High Sodium Diet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55 ^[4]	55 ^[5]		
Units: mg				
median (inter-quartile range (Q1-Q3))	-106.6 (-181.4 to -69.1)	-13 (-115.2 to 116.6)		

Notes:

[4] - 1 withdrew consent during the washout period

[5] - 2 withdrew consent and 1 violated protocol during the period 1

Statistical analyses

No statistical analyses for this end point

Post-hoc: Changes in UAE at the end of the treatment period 3 (1 month) as compared to baseline in patients on Stratum Low Sodium or High Sodium independently of treatment allocation to Placebo or Paricalcitol

End point title	Changes in UAE at the end of the treatment period 3 (1 month) as compared to baseline in patients on Stratum Low Sodium or High Sodium independently of treatment allocation to Placebo or Paricalcitol
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End point description:

End point type	Post-hoc
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End point timeframe:

Baseline to end of third month of treatment.

End point values	Low Sodium Diet	High Sodium Diet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53 ^[6]	55		
Units: mg				
median (inter-quartile range (Q1-Q3))	-273.6 (-385.9 to -151.2)	20.2 (-128.2 to 93.6)		

Notes:

[6] - 2 lost to follow-up during the third period

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The adverse events will be reported during whole study up to 30 days after last dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Patients received Placebo tablets twice daily for 1 month, regardless of sequence.

Reporting group title	Paricalcitol
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Reporting group description:

Patients received Paricalcitol 1 microgram tablets twice daily for 1 month, regardless of sequence.

Serious adverse events	Placebo	Paricalcitol	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Ischaemic heart disease			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stroke			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	
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: 0 %

Non-serious adverse events	Placebo	Paricalcitol	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 115 (31.30%)	51 / 115 (44.35%)	
Vascular disorders			

Hypotension subjects affected / exposed occurrences (all)	2 / 115 (1.74%) 2	0 / 115 (0.00%) 0	
General disorders and administration site conditions Tinnitus, hands tingling, or dizziness subjects affected / exposed occurrences (all) Fever or asthenia (unspecified) subjects affected / exposed occurrences (all)	2 / 115 (1.74%) 2 0 / 115 (0.00%) 0	1 / 115 (0.87%) 1 2 / 115 (1.74%) 2	
Immune system disorders Allergic reactions, urticaria, or pruritus subjects affected / exposed occurrences (all)	1 / 115 (0.87%) 1	1 / 115 (0.87%) 1	
Respiratory, thoracic and mediastinal disorders Flu-like symptoms, cough, bronchitis, or synusitis subjects affected / exposed occurrences (all)	2 / 115 (1.74%) 2	7 / 115 (6.09%) 7	
Cardiac disorders Legs oedema subjects affected / exposed occurrences (all)	0 / 115 (0.00%) 0	1 / 115 (0.87%) 1	
Nervous system disorders Headache or migraine subjects affected / exposed occurrences (all)	1 / 115 (0.87%) 1	2 / 115 (1.74%) 2	
Blood and lymphatic system disorders Thrombocytopenia or anaemia subjects affected / exposed occurrences (all)	2 / 115 (1.74%) 2	1 / 115 (0.87%) 1	
Gastrointestinal disorders Gastroenteritis, diarrhoea, or abdominal pain subjects affected / exposed occurrences (all) Worsening symptoms of ulcerous colitis	1 / 115 (0.87%) 1	2 / 115 (1.74%) 2	

subjects affected / exposed occurrences (all)	0 / 115 (0.00%) 0	1 / 115 (0.87%) 1	
Skin and subcutaneous tissue disorders Hypophosphaturia subjects affected / exposed occurrences (all)	2 / 115 (1.74%) 2	2 / 115 (1.74%) 2	
Dermatitis and skin infection subjects affected / exposed occurrences (all)	0 / 115 (0.00%) 0	2 / 115 (1.74%) 2	
Renal and urinary disorders Urinary tract infection or macrohaematuria subjects affected / exposed occurrences (all)	2 / 115 (1.74%) 2	1 / 115 (0.87%) 1	
Endocrine disorders Low serum iPTH concentration subjects affected / exposed occurrences (all)	0 / 115 (0.00%) 0	3 / 115 (2.61%) 3	
Musculoskeletal and connective tissue disorders Lumbar pain or cramps subjects affected / exposed occurrences (all)	0 / 115 (0.00%) 0	2 / 115 (1.74%) 2	
Osteoarthritis and trigger finger subjects affected / exposed occurrences (all)	0 / 115 (0.00%) 0	1 / 115 (0.87%) 2	
Traumatic pain or tendon tear subjects affected / exposed occurrences (all)	1 / 115 (0.87%) 1	1 / 115 (0.87%) 1	
Infections and infestations Herpes zoster infection subjects affected / exposed occurrences (all)	0 / 115 (0.00%) 0	1 / 115 (0.87%) 1	
Metabolism and nutrition disorders Hypercalciuria subjects affected / exposed occurrences (all)	1 / 115 (0.87%) 1	14 / 115 (12.17%) 14	
Hypocalciuria			

subjects affected / exposed	11 / 115 (9.57%)	3 / 115 (2.61%)	
occurrences (all)	11	3	
Hyperphosphaturia			
subjects affected / exposed	6 / 115 (5.22%)	2 / 115 (1.74%)	
occurrences (all)	6	2	
Hypercalcaemia			
subjects affected / exposed	0 / 115 (0.00%)	6 / 115 (5.22%)	
occurrences (all)	0	6	
Hyperphosphataemia			
subjects affected / exposed	0 / 115 (0.00%)	5 / 115 (4.35%)	
occurrences (all)	0	5	
Hypokalaemia, hyperhomocysteinemia, or low bone alkaline phosphate concentration			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	
occurrences (all)	1	2	
Hypocalcaemia			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	
occurrences (all)	2	0	
Hypophosphataemia			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/29104158>