



Clinical trial results:

**Primary hyperparathyroidism: does a systematic treatment improve the calcium- and bone metabolism after successful surgery? – Part
Systematic treatment of osteopenic and osteoporotic postmenopausal patients after successful surgical treatment for primary hyperparathyroidism with Strontium ranelate**

Summary

EudraCT number	2008-001703-32
Trial protocol	AT
Global end of trial date	31 January 2015

Results information

Result version number	v1 (current)
This version publication date	13 February 2019
First version publication date	13 February 2019

Trial information

Trial identification

Sponsor protocol code	PHPT_001/08
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01222026
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Medical University of Vienna
Sponsor organisation address	Waehringer Guertel 18-20, Vienna, Austria, 1090
Public contact	Martin Niederle, MD, Department of Surgery - Medical University of Vienna Prof. Bruno Niederle, MD, +43 1 40400 56210, martin.niederle@meduniwien.ac.at
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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	01 August 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 January 2015
Global end of trial reached?	Yes
Global end of trial date	31 January 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the effect of Strontium ranelate and Calcium/Vitamin D on bone density and metabolism in patients after surgical cure of primary hyperparathyroidism.

Protection of trial subjects:

All patients are monitored during routine investigations on a regular base. All subjects experiencing adverse events – whether considered associated with the study therapy or not – will be monitored until symptoms subside and any abnormal laboratory values have returned to baseline, or until there is a satisfactory explanation for the changes observed, or until death, in which case a full pathologist's report will be supplied, if possible. All findings must be reported on an „Adverse event“ page in the case report form.

All subjects names will be kept secret in the investigator's files. Subjects will be identified throughout documentation and evaluation by the number allotted to them during the study. The subjects will be told that all study findings will be stored and handled in strictest confidence.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 November 2010
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	Austria: 66
Worldwide total number of subjects	66
EEA total number of subjects	66

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)	32
From 65 to 84 years	34
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period: 2010/11/10 until 2013/12/31 (38 months)

Participants will be recruited by the Department of Surgery, Medical University of Vienna

Pre-assignment

Screening details:

All postmenopausal women and men with biochemically proven pHPT and osteopenia (t-score < -1 and > -2.5) or osteoporosis (t-score ≤ -2.5) visiting the Department of Surgery, Medical University of Vienna, between October 2010 and December 2013 were asked to participate in this study before PTX. Totally 358 patients were screened.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

Medication was coded and randomly numbered by the provider (Servier), delivered to the study center and then handed to the participants by the care providers in chronologic order (both kept blind, no special allocation to intervention groups but randomness).

All participants, care providers and those assessing outcomes were kept blind until completion of data input at the end of the follow-up period. Then the medications' codes were received from the provider and the trial was unblinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment

Arm description:

Receiving Strontium ranelate 2g per day + 1000mg Calcium + 800 IE Vitamin D

Arm type	Active comparator
Investigational medicinal product name	Strontium ranelate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules and solvent for oral suspension
Routes of administration	Oral use

Dosage and administration details:

2g daily for one year

Arm title	Placebo
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Arm description:

Receiving Placebo + 1000mg Calcium + 800 IE Vitamin D

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules for oral solution in sachet
Routes of administration	Oral use

Dosage and administration details:

Placebo granules for 1 year

Number of subjects in period 1	Treatment	Placebo
Started	34	32
Completed	29	23
Not completed	5	9
Adverse event, non-fatal	2	3
Lost to follow-up	1	2
Protocol deviation	2	4

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	66	66	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Of all participants incl. those not finishing the trial (Final calculations were done as per protocol analysis)			
Units: years			
arithmetic mean	63		
standard deviation	± 11	-	
Gender categorical			
Of all participants incl. those not finishing the trial (Final calculations were done as per protocol analysis)			
Units: Subjects			
Female	25	25	
Male	41	41	

End points

End points reporting groups

Reporting group title	Treatment
Reporting group description:	
Receiving Strontium ranelate 2g per day + 1000mg Calcium + 800 IE Vitamin D	
Reporting group title	Placebo
Reporting group description:	
Receiving Placebo + 1000mg Calcium + 800 IE Vitamin D	

Primary: %-change BMD lumbar spine

End point title	%-change BMD lumbar spine
End point description:	
End point type	Primary
End point timeframe:	
1-year-control after starting to take study medication (end of intervention)	

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	23		
Units: percent				
arithmetic mean (standard deviation)	9.94 (± 6.33)	3.94 (± 4.49)		

Statistical analyses

Statistical analysis title	t-test %-change BMD lumbar spine
Comparison groups	Treatment v Placebo
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	t-test, 2-sided

Primary: %-change BMD femoral neck

End point title	%-change BMD femoral neck
End point description:	
End point type	Primary

End point timeframe:

1-year-control after starting to take study medication (end of intervention)

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	23		
Units: percent				
arithmetic mean (standard deviation)	5.87 ($\pm$ 5.86)	4.84 ($\pm$ 4.55)		

Statistical analyses

Statistical analysis title	t-test %-change BMD femoral neck
Comparison groups	Treatment v Placebo
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.504
Method	t-test, 2-sided

Primary: %-change BMD radius 1/3

End point title	%-change BMD radius 1/3
End point description:	
End point type	Primary
End point timeframe:	
1-year-control after starting to take study medication (end of intervention)	

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	23		
Units: percent				
arithmetic mean (standard deviation)	0.42 ($\pm$ 4.06)	0.00 ($\pm$ 3.36)		

Statistical analyses

Statistical analysis title	t-test %-change BMD radius 1/3
Comparison groups	Treatment v Placebo

Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.69
Method	t-test, 2-sided

Primary: %-change BMD radius MID

End point title	%-change BMD radius MID
End point description:	
End point type	Primary
End point timeframe:	
1-year-control after starting to take study medication (end of intervention)	

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	23		
Units: percent				
arithmetic mean (standard deviation)	1.64 (± 3.23)	0.41 (± 2.86)		

Statistical analyses

Statistical analysis title	t-test %-change BMD radius MID
Comparison groups	Treatment v Placebo
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.166
Method	t-test, 2-sided

Primary: %-change BMD radius UD

End point title	%-change BMD radius UD
End point description:	
End point type	Primary
End point timeframe:	
1-year-control after starting to take study medication (end of intervention)	

End point values	Treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	23		
Units: percent				
arithmetic mean (standard deviation)	3.02 ($\pm$ 5.86)	1.84 ($\pm$ 5.76)		

Statistical analyses

Statistical analysis title	t-test %-change BMD radius UD
Comparison groups	Treatment v Placebo
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.474
Method	t-test, 2-sided

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

1-year treatment period

Assessment type	Systematic
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Dictionary used

Dictionary name	icd
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Dictionary version	10
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Reporting groups

Reporting group title	Treatment
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Reporting group description:

Receiving Strontium ranelate 2g per day + 1000mg Calcium + 800 IE Vitamin D

Reporting group title	Placebo
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Reporting group description:

Receiving Placebo + 1000mg Calcium + 800 IE Vitamin D

Serious adverse events	Treatment	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Treatment	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 32 (0.00%)	0 / 30 (0.00%)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious adverse event exceeded the threshold-rate of 5% in both groups

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 April 2013	In accordance with European Medicines Agency regulations, additional exclusion criteria (ischemic cardiac disease, peripheral arterial obstructive disease, cerebrovascular disease, and uncontrolled arterial hypertonia) were added in April 2013. Since then, electrocardiograms were included in pre-study screening and were also performed after the 12-month study period.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported