



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 |
|-----------------------|-------------|

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 |
| Scientific contact | Martin Niederle, MD, Department of Surgery - Medical University of Vienna Prof. Bruno Niederle, MD, +43 1 40400 56210, martin.niederle@meduniwien.ac.at |

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 |
|------------------|---------|

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 |
|-----------------|------------|

Dictionary used

| | |
|-----------------|-----|
| Dictionary name | icd |
|-----------------|-----|

| | |
|--------------------|----|
| Dictionary version | 10 |
|--------------------|----|

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

| 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