



Clinical trial results:

Treatment of osteopenia with melatonin: Effects on BMD, muscle strength and quality of life

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2011-004670-28 |
| Trial protocol | DK |
| Global end of trial date | 17 December 2015 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 30 August 2017 |
| First version publication date | 30 August 2017 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 2011-AKA |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01690000 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Aarhus Universitetshospital, MEA |
| Sponsor organisation address | Tage-Hansens Gade 2, Aarhus C, Denmark, 8000 |
| Public contact | Osteoporoseklinikken, Osteoporoseklinikken, 0045 7846 7681 , annekristineamstrup@gmail.dk |
| Scientific contact | Osteoporoseklinikken, Osteoporoseklinikken, 0045 7846 7681 , annekristineamstrup@gmail.dk |

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 | 17 December 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 17 December 2015 |
| Global end of trial reached? | Yes |
| Global end of trial date | 17 December 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The aim of the study is to assess the effect of melatonin treatment in patients with osteopenia on BMD, muscle function, quality of life and calcium homeostasis.

Protection of trial subjects:

Clinical visits

Blood analysis

Muscle function test

Balance function test

Background therapy:

Calcium and Vitamin D supplementation

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 14 November 2012 |
| 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 | Denmark: 81 |
| Worldwide total number of subjects | 81 |
| EEA total number of subjects | 81 |

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) | 40 |
| From 65 to 84 years | 41 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Recruitment from November 2012 to April 2013

Active Comparator: 1 mg melatonin nightly

Intervention: Drug: Melatonin

Active Comparator: 3 mg melatonin given nightly

Intervention: Drug: Melatonin

Active Comparator: Placebo

Identical placebo given nightly

Pre-assignment

Screening details:

Postmenopausal women between 55 and 75 years.

Osteopenia verified by DXA-scans of total hip or lumbar spine (t-score between -1 and -2.5)

Written informed consent after oral and written information

Period 1

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

Blinding implementation details:

A restricted block randomization was performed. Groups of eight individuals were included in the blocks. Four participants were randomly allocated to placebo, while two others received 1 mg of melatonin, and 2 received 3 mg of melatonin

Arms

| | |
|------------------------------|---------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Melatonin 1+3 |

Arm description:

1 mg melatonin or 3 mg of melatonin nightly

Intervention: Drug: Melatonin

| | |
|--|------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Melatonin 1 mg og 3 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

1mg or 3mg administrated nightly

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Identical placebo given nightly

| | |
|----------|---------|
| 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:

Given nightly

| Number of subjects in period 1 | Melatonin 1+3 | Placebo |
|---------------------------------------|---------------|---------|
| Started | 40 | 41 |
| Completed | 37 | 35 |
| Not completed | 3 | 6 |
| Adverse event, non-fatal | 2 | 1 |
| Protocol deviation | 1 | 5 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | Melatonin 1+3 |
|-----------------------|---------------|

Reporting group description:

1 mg melatonin or 3 mg of melatonin nightly

Intervention: Drug: Melatonin

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Identical placebo given nightly

| Reporting group values | Melatonin 1+3 | Placebo | Total |
|--|---------------|---------|-------|
| Number of subjects | 40 | 41 | 81 |
| Age categorical | | | |
| Women between 55-75 | | | |
| 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) | 32 | 29 | 61 |
| From 65-84 years | 8 | 12 | 20 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Women between 55-75 years | | | |
| Units: years | | | |
| arithmetic mean | 62.9 | 62.4 | |
| standard deviation | ± 4.5 | ± 3.5 | - |
| Gender categorical | | | |
| Only women could participate | | | |
| Units: Subjects | | | |
| Female | 40 | 41 | 81 |
| Male | 0 | 0 | 0 |

End points

End points reporting groups

| | |
|--|---------------|
| Reporting group title | Melatonin 1+3 |
| Reporting group description: 1 mg melatonin or 3 mg of melatonin nightly Intervention: Drug: Melatonin | |
| Reporting group title | Placebo |
| Reporting group description: Identical placebo given nightly | |

Primary: Changes in BMD

| | |
|---|----------------|
| End point title | Changes in BMD |
| End point description: | |
| End point type | Primary |
| End point timeframe: After 12 months treatment -end of study | |

| End point values | Melatonin 1+3 | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 39 | 37 | | |
| Units: Percent | 39 | 37 | | |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | T-test |
| Comparison groups | Melatonin 1+3 v Placebo |
| Number of subjects included in analysis | 76 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | t-test, 2-sided |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 1.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 2.7 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

2012 to 2014

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

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 19 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | Melatonin 1+3 |
|-----------------------|---------------|

Reporting group description:

Receiving either 1 or 3 mg melatonin

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Received placebo nightly

| Serious adverse events | Melatonin 1+3 | Placebo | |
|---|---|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 40 (12.50%) | 7 / 41 (17.07%) | |
| 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) | | | |
| Cancer surgery | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 3 / 41 (7.32%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Venous thrombosis | Additional description: Thrombosis after knee surgery | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 41 (2.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Operation | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 41 (2.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Arrhythmia | Additional description: arrhythmia | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 40 (2.50%) | 2 / 41 (4.88%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Planned Operation | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 1 / 41 (2.44%) | |
| occurrences causally related to treatment / all | 0 / 2 | 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 | Melatonin 1+3 | Placebo | |
|---|--------------------------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 19 / 40 (47.50%) | 19 / 41 (46.34%) | |
| Cardiac disorders | | | |
| Tachycardia | Additional description: tachycardia | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 1 / 41 (2.44%) | |
| occurrences (all) | 1 | 1 | |
| Ear and labyrinth disorders | | | |
| Dizziness | Additional description: and headache | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 1 / 41 (2.44%) | |
| occurrences (all) | 2 | 1 | |
| Immune system disorders | | | |
| Allergy | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 41 (2.44%) | |
| occurrences (all) | 0 | 1 | |
| Social circumstances | | | |
| Abnormal dreams | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 41 (2.44%) | |
| occurrences (all) | 0 | 1 | |
| others | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 41 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |

| | | | |
|---|-------------------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 | 0 / 41 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders airway infection subjects affected / exposed occurrences (all) | 2 / 40 (5.00%) 2 | 3 / 41 (7.32%) 3 | |
| Cough | Additional description: cough | | |
| subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 | 0 / 41 (0.00%) 0 | |
| Skin and subcutaneous tissue disorders Skin discomfort subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 | 0 / 41 (0.00%) 0 | |
| Renal and urinary disorders urigenital matters subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 | 3 / 41 (7.32%) 3 | |
| Musculoskeletal and connective tissue disorders Pain subjects affected / exposed occurrences (all) | 5 / 40 (12.50%) 5 | 6 / 41 (14.63%) 6 | |
| Infections and infestations Infection subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 | 1 / 41 (2.44%) 1 | |

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