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