Clinical trial results:
The Relationship between Osteoporosis and Aortic Calcification in Postmenopausal Women

Summary

EudraCT number	2008-001865-28
Trial protocol	GB
Global end of trial date	24 October 2014

Results information

Result version number	v1 (current)
This version publication date	08 November 2018
First version publication date	08 November 2018
Summary attachment (see zip file)	FINAL STUDY REPORT (Clinical study report_MHRA signed.pdf)

Trial information

Trial identification

Sponsor protocol code	08/H0802/9

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	King's College London
Sponsor organisation address	The Strand, London, United Kingdom, WC2R 2LS
Public contact	Osteoporosis Unit , King's College London, 0044 207 1887188,
Scientific contact	Osteoporosis Unit , King's College London, 0044 207 1887188,
Sponsor organisation name	Guy's and St Thomas' NHS Foundation Trust
Sponsor organisation address	Great Maze Pond, London, United Kingdom, SE19RT
Public contact	Osteoporosis Unit, King's College London, 0044 2071887188, michelle.frost@kcl.ac.uk
Scientific contact	Osteoporosis Unit, King's College London, 0044 2071887188, michelle.frost@kcl.ac.uk

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	24 October 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 October 2014
Global end of trial reached?	Yes
Global end of trial date	24 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effects of bisphosphonate alendronate on aortic calcification in postmenopausal women with osteoporosis and severe osteopenia.

Protection of trial subjects:

Informed consent will be obtained before any screening procedures are performed

Background therapy:

None

Evidence for comparator: -

Actual start date of recruitment	01 July 2008
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	United Kingdom: 26
Worldwide total number of subjects	26
EEA total number of subjects	26

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)	20
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Thirty subjects were recruited on to this part of the study, although 6 subjects failed at screening. Study subjects were randomised and divided into two groups. Participants were recruited from one clinical site in London.

Pre-assignment

Screening details:

inclusion criteria:
Ambulatory postmenopausal* women
Aged 50 years and over
Lumbar spine (L1-L4) and/or femoral neck and/or total hip BMD measurement more than 2 standard deviations below the young adult mean for healthy women (T-score ≤ -2).
Normal or clinically insignificant laboratory values

Period 1

Period 1 title	Whole Group (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This was an open label trial.

Arms

Are arms mutually exclusive?	Yes
Arm title	Interventional

Arm description:

Once weekly alendronate 70mg for 2-years and daily calcium and vitamin D supplementation providing 600mg/400IU of calcium and vitamin D.

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

Dosage and administration details:

Once weekly alendronate 70mg for 2-years and daily calcium and vitamin D supplementation providing 600mg/400IU of calcium and vitamin D

Investigational medicinal product name	Calcium & Vitamin D
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

daily calcium and vitamin D supplementation providing 600mg/400IU of calcium and vitamin D..

Arm title	Control Group

Arm description:

Participants prescribed calcium and vitamin D supplements providing 600mg/400IU of calcium and vitamin D

Arm type	CONTROL

Investigational medicinal product name	calcium and vitamin D
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

12 controls that were only given calcium and vitamin D supplements providing 600mg/400IU of calcium and vitamin D. The study subjects attended for a total of 7 visits over 2-years.

Number of subjects in period 1	Interventional	Control Group
Started	14	12
Completed	12	10
Not completed	2	2
Lost to follow-up	2	2

Baseline characteristics

End points

End points reporting groups

Reporting group title	Interventional

Reporting group description:

Once weekly alendronate 70mg for 2-years and daily calcium and vitamin D supplementation providing 600mg/400IU of calcium and vitamin D.

Reporting group title	Control Group

Reporting group description:

Participants prescribed calcium and vitamin D supplements providing 600mg/400IU of calcium and vitamin D

Primary: Clinical Endpoint

End point title	Clinical Endpoint[1]

End point description:

To evaluate the effects of bisphosphonate alendronate on aortic calcification in postmenopausal women with osteoporosis and severe osteopenia

End point type	Primary

End point timeframe:

Duration of the trial

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Please see attached report for full results.

End point values	Interventional	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	10		
Units: whole	12	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Endpoint

End point title	Clinical Endpoint

End point description:

To examine the relationship between BMD and aortic calcification

End point type	Secondary

End point timeframe:

Duration of trial

End point values	Interventional	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	10		
Units: whole	12	10		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Duration of Trial	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1
Reporting groups	
Reporting group title	Interventional Arm
Reporting group description: -	
Reporting group title	Control Arm
Reporting group description: -	

Serious adverse events	Interventional Arm	Control Arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Interventional Arm	Control Arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	9 / 10 (90.00%)	
Surgical and medical procedures			
Angiogram			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Cholesytectomy & gall stones removed			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Colonoscopy			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Crown replacement			

subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Curettage			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Filling			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Hip replacement			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Removal of papilloma from buttock			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Removal of right ingrown eyelash			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	2	
Retinal attachment operation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Root canal			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Dental examination abnormal			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Tooth implant			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
General malaise			

subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Tooth ache			
subjects affected / exposed	1 / 12 (8.33%)	2 / 10 (20.00%)	
occurrences (all)	1	2	
Reproductive system and breast disorders			
Vaginal atrophy			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Recurrence of post-menopausal bleed			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Fibroids			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Apical pleural thickening			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Breathlessness (climbing stairs)			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Cold			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Cough			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Dyspnoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Fever/coughing/general malaise			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Inflammatory lung nodule			

subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Loss of voice			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Parenchymal lung nodule			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Peripheral lung nodule			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	
occurrences (all)	2	1	
Pleural effusion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Pleural nodularity in lung bases			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Precordial tightness			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Recurence of asthma			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Retroperitoneal calcification to Hilium			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Small peripheral lung nodule			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Sore throat			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	
occurrences (all)	4	1	
Thoracic pleural thickening			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			

subjects affected / exposed	4 / 12 (33.33%)	2 / 10 (20.00%)	
occurrences (all)	7	3	
Wheezing and coughin			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Psychiatric disorders			
Mild depression/low mood			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Food poisoning			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	2	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 12 (16.67%)	2 / 10 (20.00%)	
occurrences (all)	2	2	
Migraine			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Bilateral axillary adenopathy			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Mild lymphocytic lymphoma/CLL			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Possible lymph nodes sternoclavicular			

subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Calcification at splenic hilum			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Mediastinal adenopathy			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Adenopathy with mesenteric stranding			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Thickness in ear			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Vision loss			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Increase in ophthalmic pressure			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Eye pain/irritation			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
Acid reflux & oesophageal discomfort			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Bloating of abdomen			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			

subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	
occurrences (all)	2	1	
Indigestion			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Nausea			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Norovirus			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	
occurrences (all)	3	1	
Stomach pain			
subjects affected / exposed	1 / 12 (8.33%)	2 / 10 (20.00%)	
occurrences (all)	1	7	
Gastric Upset			
subjects affected / exposed	0 / 12 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	3	
Hepatobiliary disorders			
Liver cysts			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Gallstones			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Insect bites on leg			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Urinary Tract infection			
subjects affected / exposed	3 / 12 (25.00%)	1 / 10 (10.00%)	
occurrences (all)	12	2	
Renal calculus			

subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Urinary incontinence when walking fast			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Thyroid nodule			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Adrenal adenoma			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	3 / 12 (25.00%)	1 / 10 (10.00%)	
occurrences (all)	4	1	
Broken rib			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Chest pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Cold fingertips			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Broken finger			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Fractured metatarsal in foot			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Grade 1 anterolisthesis of L5 on S1			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Frozen shoulder			

subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Hip Pain			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Increase in stiffness (knees/ankle)			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Intervertebral height loss			
subjects affected / exposed	0 / 12 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	
Loss of joint space at hip			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Multi-focal end plate thickening			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Neck pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Painful knee			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Joint pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Painful shoulder			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Painful thumb joint			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Paresthesia in scapula			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Rib pain			

subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Shortening of left leg length			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Shoulder and neck pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Shoulder pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Tennis elbow			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Vertebral body degeneration			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Genital Herpes			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Endobronchial infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 October 2009	Change of Chief Investigator and classification of part of this trial.
19 January 2012	Amendment to protocol sample size from 50 to 26 participants

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
25 August 2009	Change of Chief Investigator and classification of part of the trial	14 October 2009

Notes:

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27572995