



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
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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 $\leq$ -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
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Arm description:

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

Arm type	CONTROL
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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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	Interventional Arm
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Reporting group description: -

Reporting group title	Control Arm
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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	
Cholecystectomy & 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 occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	
Tooth ache subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	2 / 10 (20.00%) 2	
Reproductive system and breast disorders			
Vaginal atrophy subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	
Recurrence of post-menopausal bleed subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	
Fibroids subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	
Respiratory, thoracic and mediastinal disorders			
Apical pleural thickening subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	
Breathlessness (climbing stairs) subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	
Cold subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	0 / 10 (0.00%) 0	
Cough subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 10 (10.00%) 1	
Dyspnoea subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	
Fever/coughing/general malaise subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 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
Recurrence of asthma		
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	1
Retroperitoneal calcification to Hilum		
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 occurrences (all)	4 / 12 (33.33%) 7	2 / 10 (20.00%) 3	
Wheezing and coughin subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	
Psychiatric disorders Mild depression/low mood subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	
Injury, poisoning and procedural complications Food poisoning subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 2	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	2 / 10 (20.00%) 2	
Migraine subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	
Blood and lymphatic system disorders Bilateral axillary adenopathy subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	
Mild lymphocytic lymphoma/CLL subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	
Hypertension subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	
Possible lymph nodes sternoclavicular			

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

subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	1 / 10 (10.00%) 1	
Indigestion subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 10 (10.00%) 1	
Nausea subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	
Norovirus subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	
Vomiting subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 3	1 / 10 (10.00%) 1	
Stomach pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	2 / 10 (20.00%) 7	
Gastric Upset subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	2 / 10 (20.00%) 3	
Hepatobiliary disorders Liver cysts subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	
Gallstones subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	
Skin and subcutaneous tissue disorders Insect bites on leg subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	
Renal and urinary disorders Urinary Tract infection subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 12	1 / 10 (10.00%) 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 occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	
Shortening of left leg length subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	
Shoulder and neck pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	
Shoulder pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	
Tennis elbow subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	
Vertebral body degeneration subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0	
Infections and infestations			
Genital Herpes subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 10 (10.00%) 1	
Endobronchial infection subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 10 (0.00%) 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>