Clinical trial results:
Improving the outcome for elderly patients after osteoporotic femoral fractures

Summary

EudraCT number	2009-015058-38
Trial protocol	GB
Global end of trial date	05 February 2014

Results information

Result version number	v1 (current)
This version publication date	20 March 2020
First version publication date	20 March 2020
Summary attachment (see zip file)	OFF trial Summary (2020.03.04_NOF publication sent to Clare.pdf)

Trial information

Trial identification

Sponsor protocol code	OR09/9018

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University of Leeds
Sponsor organisation address	Worsley Building, Leeds, United Kingdom, LS2 9JT
Public contact	Professor P.V. Giannoudis, University of Leeds, 0113 2067068, P.Giannoudis@leeds.ac.uk
Scientific contact	Professor P.V. Giannoudis, University of Leeds, 0113 2067068, P.Giannoudis@leeds.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	05 February 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 February 2014
Global end of trial reached?	Yes
Global end of trial date	05 February 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To produce preliminary evidence testing the hypothesis that it is possible to accelerate the healing of trochanteric and distal femoral fractures with the administration of therapeutic agents (Parathyroid Hormone, Biphosphonate, Vitamin D and Calcium) and thus reduce pain and functional impairment at 3 and 6months.

Protection of trial subjects:

The trial was conducted in accordance with GCP and the EU clinical trials regulation, was carried out under a Clinical Trial Authorisation, and the Local REC approved the study. The trial was also independently monitored by the Sponsor.To comply with regulations, all essential source and study documentation will be securely retained for at least 15 years.

Background therapy:

Osteoporosis is a common disease in the elderly and the fractures that result from this disorder affect 40% of women and 14 % of men over the age of 50 years.1 Osteoporosis is characterised by loss of trabecular bone mass and connectivity, as well as thinning of cortical bone.2 Low bone mineral density in the elderly can result from either low peak bone mass, or accelerated bone loss, or a combination of the two. A strong genetic component has also been suggested to contribute to the pathogenesis of osteoporotic fractures.3, 4, 5
With the increasing number of elderly people it is anticipated that this disease process will become an epidemic in the years to come. Indeed, statistics predict that by the year 2012, 25% of the European Population will be over the age of 65 and by year 2020 over 52 million will be over 65 years old in the USA.6 In the UK in particular, according to the 2001 census, elderly over 60 years of age outnumbered the under 16 years old for the first time and elderly over 85 increased 5 fold since 1951. The elderly patient therefore will increasingly consume more hospital resources than patients from any other group especially for the treatment of fractures of both the upper and lower extremity as a result of bone fragility.

Evidence for comparator: -

Actual start date of recruitment	11 April 2011
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: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	0
From 65 to 84 years	30
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A 1-year recruitment period will be allowed. Each patient will be recruited and have to start treatment within one week from surgery.Patients will be recruited at Leeds. This tertiary referral trauma centre admits over 500 hip fractures each yea rand therefore, has a large clinical base to participate in this study.

Pre-assignment

Screening details:

Patients with a broken Femur caused by Osteoporosis were identified in Clinic, and provided with a copy of the PIS. It was made clear to participants could withdraw at any time.

Period 1

Period 1 title	Main Trial Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment A: Anti-resorptive agent - Biphosphonates

Arm description:

Treatment A: Anti-resorptive agent - Biphosphonates (Alendronate)
Fosamax 70 mg tablets (Merck)

Arm type	Experimental
Investigational medicinal product name	Fosamax 70mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

70mg to be taken, two tablets daily

Arm title	Anabolic agent - Parathyroid hormone

Arm description:

Patients will receive 20 micrograms of teriparatide (Forsteo) given daily by subcutaneous injection for 4 weeks. This will be supplemented by administration of Vitamin D (800 iu/daily) and Calcium (1.200 mg/daily of elemental calcium) for the same time period, which will be preferably the tablets will be taken once daily.

Arm type	Experimental
Investigational medicinal product name	teriparatide (Forsteo)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients will receive 20 micrograms of teriparatide (Forsteo) given daily by subcutaneous injection for 4 weeks. This will be supplemented by administration of Vitamin D (800 iu/daily) and Calcium (1.200 mg/daily of elemental calcium) for the same time period,which will be preferably the tablets will be taken once daily.

Arm title	Control - Vitamin D and Calcium

Arm description:

Patients will receive Vitamin D (800 iu/daily) and Calcium (1.200 mg/daily of elemental calcium) in two tablets daily for 4 weeks. Preferably the tablets will be taken once daily.

Arm type	Control
Investigational medicinal product name	Vitamin D and Calcium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients will receive Vitamin D (800 iu/daily) and Calcium (1.200 mg/daily of elemental calcium) in two tablets daily for 4 weeks. Preferably the tablets will be taken once daily.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: The data analysts were blinded to the identity of the treatment from the time of randomisation. The Department of Clinical Trials of our local pharmacy (Leeds General Infirmary) was responsible for supplying, packaging and labelling the investigational and control drugs, as well as for the randomisation of the recruited patients to the different study groups.

Number of subjects in period 1	Treatment A: Anti-resorptive agent - Biphosphonates	Anabolic agent - Parathyroid hormone	Control - Vitamin D and Calcium
Started	11	9	10
Completed	8	6	5
Not completed	3	3	5
Consent withdrawn by subject	3	3	5

Baseline characteristics

Reporting groups

Reporting group title	Main Trial Period

Reporting group description: -

Reporting group values	Main Trial Period	Total	
Number of subjects	30	30	
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 Units: years			
arithmetic mean	75		
standard deviation	± 8.89	-	
Gender categorical Units: Subjects			
Female	24	24	
Male	6	6	

End points

End points reporting groups

Reporting group title	Treatment A: Anti-resorptive agent - Biphosphonates
Reporting group description:	
Treatment A: Anti-resorptive agent - Biphosphonates (Alendronate) Fosamax 70 mg tablets (Merck)	
Reporting group title	Anabolic agent - Parathyroid hormone
Reporting group description:	
Patients will receive 20 micrograms of teriparatide (Forsteo) given daily by subcutaneous injection for 4 weeks. This will be supplemented by administration of Vitamin D (800 iu/daily) and Calcium (1.200 mg/daily of elemental calcium) for the same time period, which will be preferably the tablets will be taken once daily.	
Reporting group title	Control - Vitamin D and Calcium
Reporting group description:	
Patients will receive Vitamin D (800 iu/daily) and Calcium (1.200 mg/daily of elemental calcium) in two tablets daily for 4 weeks. Preferably the tablets will be taken once daily.	

Primary: Pain Reduction and functional impairment at 3-6 months Post operative

End point title	Pain Reduction and functional impairment at 3-6 months Post operative[1]
End point description:	
End point type	Primary
End point timeframe:	
3-6 months Post operative.	

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: No meaningful statistical comparative analysis was possible due to the small sample that was possible to enrol and follow up, as this pilot randomized clinical trial was closed due to limited recruitment rates and funding resources.

End point values	Treatment A: Anti-resorptive agent - Biphosphonates	Anabolic agent - Parathyroid hormone	Control - Vitamin D and Calcium	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[2]	0[3]	0[4]	
Units: yes/no				

Notes:

[2] - No meaningful statistical comparative analysis was possible due to the small sample
[3] - No meaningful statistical comparative analysis was possible due to the small sample
[4] - No meaningful statistical comparative analysis was possible due to the small sample

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

All AEs will be recorded on the appropriate CRF with the following information:
1. the severity grade (mild, moderate, severe)
2. its relationship to the study drug(s) (suspected/not suspected)
3. whether it constitutes a serious adverse event (SAE)

Adverse event reporting additional description:

All SAEs will be reported by the Principal Investigator (PI) or Trial Coordinator within 24 hours of being made aware of the event. The PI will record the event with an assessment of seriousness, causality, expectedness and severity on an SAE form. The PI will also ensure that follow-up information is provided when available.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	Treatment A: Anti-resorptive agent - Biphosphonates

Reporting group description:

Treatment A: Anti-resorptive agent - Biphosphonates (Alendronate)
Fosamax 70 mg tablets (Merck)

Reporting group title	Anabolic agent - Parathyroid hormone

Reporting group description:

Patients will receive 20 micrograms of teriparatide (Forsteo) given daily by subcutaneous injection for 4 weeks. This will be supplemented by administration of Vitamin D (800 iu/daily) and Calcium (1.200 mg/daily of elemental calcium) for the same time period, which will be preferably the tablets will be taken once daily.

Reporting group title	Control - Vitamin D and Calcium

Reporting group description:

Patients will receive Vitamin D (800 iu/daily) and Calcium (1.200 mg/daily of elemental calcium) in two tablets daily for 4 weeks. Preferably the tablets will be taken once daily.

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: Details of adverse events can be found in table 1 of the attached summary paper, in the 'complications' row.

Serious adverse events	Treatment A: Anti-resorptive agent - Biphosphonates	Anabolic agent - Parathyroid hormone	Control - Vitamin D and Calcium
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
number of deaths (all causes)	1	0	3
number of deaths resulting from adverse events	0	0	0
Product issues			
Implant Failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Treatment A: Anti-resorptive agent - Biphosphonates	Anabolic agent - Parathyroid hormone	Control - Vitamin D and Calcium
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 September 2010	MHRA required the clearer description of one of the exclusion criteria (regarding women of child bear age, and patients with malignancies), the revision of the dosing schemes for Calcium tablets (correction of the mgs of calcium and vitamin D to be administered - still each patient will receive 2 tablets per day as initially described), clarifications on the time endpoints of the study which now are all related to the time from surgery (T0).
12 September 2011	Amendments made to the protocol and PIS as a result of monitoring findings. PIS amended to match dosing strategy to the labels generated by the trial pharmacy department. Protocol amended to v6.0, PIS to v4.0

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
18 September 2012	Study was suspended for patient recruitment as a result of the findings uncovered as part of a Sponsor monitoring visit in September 2012. Study was monitored previously in June 2011, and the findings from the previous monitoring visit were not implemented appropriately. Study was restarted once the Sponsor determined all monitoring actions had been resolved.	26 November 2012

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Trial did not collect enough data to report on the primary endpoint of the study.

Notes: