Clinical trial results:
Denosumab in enhancement of bone bonding of hip prosthesis in postmenopausal women: a randomized, double-blind, placebo-controlled study

Summary

EudraCT number	2011-000628-14
Trial protocol	FI
Global end of trial date	17 October 2018

Results information

Result version number	v1 (current)
This version publication date	19 October 2024
First version publication date	19 October 2024
Summary attachment (see zip file)	Publication JBMR_Plus (Aro_et_al-2019-JBMR_Plus.pdf)

Trial information

Trial identification

Sponsor protocol code	ISS20109714

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01926158
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen AB
Sponsor organisation address	Keilaranta 16, Espoo, Finland, 02150
Public contact	Sivuliike Suomessa , Amgen AB, 358 954900500, paivi.lakkakorpi@amgen.com
Scientific contact	Sivuliike Suomessa , Amgen AB, 358 954900500, paivi.lakkakorpi@amgen.com

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 October 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 October 2018
Global end of trial reached?	Yes
Global end of trial date	17 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary hypothesis for this trial is that denosumab compared with placebo is effective in preventing periprosthetic bone loss in the proximal femur of female patients after total hip replacement

Protection of trial subjects:

No need of specific methods of protection

Background therapy:

No background therapy

Evidence for comparator:

Comparison with placebo

Actual start date of recruitment	01 September 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 67
Worldwide total number of subjects	67
EEA total number of subjects	67

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)	15
From 65 to 84 years	52

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment between November 2013 and June 2015

Pre-assignment

Screening details:

Postmenopausal women between 60 and 85 years of age with primary hip osteoarthritis as the indicaction for the need of hip replacement. 205 subjects assessed for eligibility. 140 excluded for the following reasons: not meeting inclusion criteria (n=63), declined to participate (n=35) and other reasons (n=42).

Pre-assignment period milestones

Number of subjects started	67
Number of subjects completed	67

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Allocated to denosumab treatment

Arm description:

Denosumab treatment (60 mg every 6 months) for one year

Arm type	Active comparator
Investigational medicinal product name	Prolia
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Epicutaneous use

Dosage and administration details:

Subcutaneous injection of denosumab 60 mg every 6 months

Arm title	Allocated to placebo

Arm description:

Placebo injection every 6 moths for one year

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection

Dosage and administration details:

Subcutaneous injection every 6 months for one year

Number of subjects in period 1	Allocated to denosumab treatment	Allocated to placebo
Started	33	34
Completed	33	32
Not completed	0	2
Consent withdrawn by subject	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Allocated to denosumab treatment
Reporting group description:	
Denosumab treatment (60 mg every 6 months) for one year	
Reporting group title	Allocated to placebo
Reporting group description:	
Placebo injection every 6 moths for one year	

Reporting group values	Allocated to denosumab treatment	Allocated to placebo	Total
Number of subjects	33	34	67
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	69	69	
standard deviation	± 5	± 6	-
Gender categorical			
Units: Subjects			
Female	33	34	67
Male	0	0	0
Low BMD			
BMD measured by DXA			
Units: Subjects			
Osteopenia	15	17	32
Osteoporosis	2	0	2
Normal BMD	16	17	33
History of low-energy fractures			
Number of subjects with a history of low-energy fractures			
Units: Subjects			
Fracture - yes	9	8	17
Fracture - no	24	26	50

End points

End points reporting groups

Reporting group title	Allocated to denosumab treatment
Reporting group description: Denosumab treatment (60 mg every 6 months) for one year	
Reporting group title	Allocated to placebo
Reporting group description: Placebo injection every 6 moths for one year	

Primary: Percentage change of periprosthetic calcar BMD (Gruen 7)

End point title	Percentage change of periprosthetic calcar BMD (Gruen 7)
End point description: Periprosthetic BMD measured by DXA immediately after fracture and at 48 weeks	
End point type	Primary
End point timeframe: During the first 48 weeks after surgery	

End point values	Allocated to denosumab treatment	Allocated to placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	32		
Units: percent				
least squares mean (confidence interval 95%)	5.3 (2.2 to 8.5)	18.1 (14.5 to 21.6)		

Attachments (see zip file)	Periprosthetic BMD after surgery/Periprosthetic BMD change.

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description: The primary and secondary endpoints (the outcome measured at week 48) were analyzed using linear mixedeffects models for repeated measures. The method was also applied to evaluate intergroup differences at each time point (12, 22, and 48 weeks) as the exploratory endpoints of the different outcome parameters. No data were excluded.	
Comparison groups	Allocated to denosumab treatment v Allocated to placebo

Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Mixed models analysis

Secondary: Implant 3D-migration

End point title	Implant 3D-migration

End point description:

Baseline RSA measurements at day 3. Measurement of 3D-translation and 3D-rotation at 12, 22 and 48 weeks.

End point type	Secondary

End point timeframe:

0, 12, 22, 48 weeks

End point values	Allocated to denosumab treatment	Allocated to placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	32		
Units: degrees				
arithmetic mean (confidence interval 95%)	2.4 (1.6 to 3.3)	2.3 (1.5 to 3.2)		

Attachments (see zip file)	Implant migration/Postop implant 3D-migration.pdf

Statistical analyses

Statistical analysis title	Statistical analysis

Statistical analysis description:

The primary and secondary endpoints (the outcome measured at week 48) were analyzed using linear mixedeffects models for repeated measures. The method was also applied to evaluate intergroup differences at each time point (12, 22, and 48 weeks) as the exploratory endpoints of the different outcome parameters. No data were excluded.

Comparison groups	Allocated to denosumab treatment v Allocated to placebo
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Mixed models analysis

Other pre-specified: Patient-reported outcome measures

End point title	Patient-reported outcome measures

End point description:	
Harris hip score, WOMAC score, Rand-36 score, BPI-pain score	
End point type	Other pre-specified
End point timeframe:	
0, 12, 22, 48 weeks	

End point values	Allocated to denosumab treatment	Allocated to placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	32		
Units: scores				
arithmetic mean (confidence interval 95%)	78 (74 to 82)	72 (68 to 76)		

Attachments (see zip file)	Patient-reported outcome measures.pdf

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description:	
The primary and secondary endpoints (the outcome measured at week 48) were analyzed using linear mixedeffects models for repeated measures. The method was also applied to evaluate intergroup differences at each time point (12, 22, and 48 weeks) as the exploratory endpoints of the different outcome parameters. No data were excluded.	
Comparison groups	Allocated to denosumab treatment v Allocated to placebo
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Mixed models analysis

Other pre-specified: Walking speed and walking activity

End point title	Walking speed and walking activity
End point description:	
Walking speed and walking activity measured repeatedly during the first year after hip replacement	
End point type	Other pre-specified
End point timeframe:	
Walking speed at 0, 3, 6, 12, 24 and 36 weeks. Walking activity measured at 3, 6, and 12 months.	

End point values	Allocated to denosumab treatment	Allocated to placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	32		
Units: m/sec or counts				
arithmetic mean (confidence interval 95%)	1.16 (1.10 to 1.23)	1.20 (1.07 to 1.24)		

Attachments (see zip file)	Walking speed and walking activity/Walking speed and walking

Statistical analyses

Statistical analysis title	Statistical analysis

Statistical analysis description:

The primary and secondary endpoints (the outcome measured at week 48) were analyzed using linear mixedeffects models for repeated measures. The method was also applied to evaluate intergroup differences at each time point (12, 22, and 48 weeks) as the exploratory endpoints of the different outcome parameters. No data were excluded.

Comparison groups	Allocated to denosumab treatment v Allocated to placebo
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Mixed models analysis

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
The first year after hip replacement	
Adverse event reporting additional description:	
The incidence of adverse events and serious adverse events	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedVED
Dictionary version	3

Reporting groups	
Reporting group title	AEs and SAEs
Reporting group description:	
The incidence of AEs and SAEs during the 1-year trial period was balanced between the two groups. The most common AE was low back pain.	

Serious adverse events	AEs and SAEs		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 65 (10.77%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Bradycardia. Mild infarct.			
subjects affected / exposed	7 / 65 (10.77%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	AEs and SAEs		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 65 (47.69%)		
Musculoskeletal and connective tissue disorders			
Low back pain			
subjects affected / exposed	31 / 65 (47.69%)		
occurrences (all)	31		

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31687650