Clinical trial results:
The PRedictive value of bOne turnover markerS during discontinuation of Alendronate: The PROSA study

Summary

EudraCT number	2016-003110-27
Trial protocol	DK
Global end of trial date	15 September 2020

Results information

Result version number	v1 (current)
This version publication date	10 December 2020
First version publication date	10 December 2020

Trial information

Trial identification

Sponsor protocol code	21.07.2016

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03051620
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Dept. of Endocrinology and Internal Medicine, Aarhus University Hospital
Sponsor organisation address	Palle Juul-Jensens Boulevard 99, Aarhus, Denmark, 8200
Public contact	Bente Lomholt Langdahl, Dept. of Endocrinology and Internal Medicine, Aarhus University Hospital , benlan@rm.dk
Scientific contact	Bente Lomholt Langdahl, Dept. of Endocrinology and Internal Medicine, Aarhus University Hospital , benlan@rm.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	15 September 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 September 2020
Global end of trial reached?	Yes
Global end of trial date	15 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary endpoint was if p-CTX measured three and six months after stopping alendronate (ALN) predicts changes in total hip BMD (THBMD) after one year.

The secondary endpoints were if baseline p-CTX, p-PINP, the ratio p-CTX/p-PINP, or changes thereof measured three and six months after stopping ALN treatment predict changes in BMD at any site after one and two years.
Additional endpoints were the proportion of the study population in which bone turnover increased above premenopausal/young adult reference levels after 3, 6, 12 and 24 months, and the proportion of the study population who lost BMD beyond the least significant change at the lumbar spine and total hip.

Protection of trial subjects:

We re-initiated alendronate if there was a rapid decrease in BMD >8% (any site), if a patient suffered a low energy fracture or if a patient with BMD T-score < -2.5 initiated daily treatment with systemic glucocorticoids.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 February 2017
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: 142
Worldwide total number of subjects	142
EEA total number of subjects	142

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)	41
From 65 to 84 years	101
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The Department of Endocrinology and Internal Medicine, Aarhus University Hospital
The Department of Internal Medicine, Horsens Regional Hospital
Advertisements in daily newspapers and online
Data extraction from The Danish Health Data Authority

Pre-assignment

Screening details:

DXA
Blood samples
Inclusions and exclusions criteria

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	study population

Arm description:

Treatment pause with alendronate

Arm type	Experimental
Investigational medicinal product name	No treatment
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Other use

Dosage and administration details:

Treatment pause with alendronate after min 5 years of treatment

Number of subjects in period 1	study population
Started	142
Completed	124
Not completed	18
Withdraw on medical grounds	8
Lost to follow-up	10

Baseline characteristics

Reporting groups	
Reporting group title	Overall period
Reporting group description:	
Study population: n=142	

Reporting group values	Overall period	Total	
Number of subjects	142	142	
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	68		
standard deviation	± 6	-	
Gender categorical Units: Subjects			
Female	122	122	
Male	20	20	

Subject analysis sets	
Subject analysis set title	Analysis plan: BMD, BTM, TBS
Subject analysis set type	Per protocol
Subject analysis set description: Paired sample-t-test Mixed model analysis of variance Stratified analyses	
Subject analysis set title	Analysis plan: correlations
Subject analysis set type	Per protocol
Subject analysis set description: Stratified analyses multiple linear regression	

Reporting group values	Analysis plan: BMD, BTM, TBS	Analysis plan: correlations	
Number of subjects	142	142	
Age categorical Units: Subjects			
In utero			

Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	68		
standard deviation	± 6	±	
Gender categorical Units: Subjects			
Female	122		
Male	20		

End points

End points reporting groups

Reporting group title	study population
Reporting group description: Treatment pause with alendronate	
Subject analysis set title	Analysis plan: BMD, BTM, TBS
Subject analysis set type	Per protocol
Subject analysis set description: Paired sample-t-test Mixed model analysis of variance Stratified analyses	
Subject analysis set title	Analysis plan: correlations
Subject analysis set type	Per protocol
Subject analysis set description: Stratified analyses multiple linear regression	

Primary: Primary endpoint

End point title	Primary endpoint
End point description: The primary endpoint was if p-CTX measured three and six months after stopping alendronate predicts changes in THBMD after one year.	
End point type	Primary
End point timeframe: 1 year	

End point values	Analysis plan: BMD, BTM, TBS	Analysis plan: correlations		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	142	142		
Units: p value				
number (not applicable)	142	142		

Statistical analyses

Statistical analysis title	Analysis plan
Statistical analysis description: Paired sample-t-test Mixed model analysis of variance Stratified analyses multiple linear regression	
Comparison groups	Analysis plan: BMD, BTM, TBS v Analysis plan: correlations

Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0 [1]
Method	Regression, Linear

Notes:

[1] - Hypothesis tested p <= 0.05

Secondary: Secondary endpoint

End point title	Secondary endpoint

End point description:

The secondary endpoints were if baseline p-CTX, p-PINP, the ratio p-CTX/p-PINP, or changes thereof measured three and six months after stopping alendronate treatment predict changes in BMD at any site after one and two years.

Additional endpoints were the proportion of the study population in which bone turnover increased above premenopausal/young adult reference levels after 3, 6, 12 and 24 months, and the proportion of the study population who lost BMD beyond the least significant change at the lumbar spine and total hip.

End point type	Secondary

End point timeframe:

one and two years

End point values	Analysis plan: BMD, BTM, TBS	Analysis plan: correlations		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	142	142		
Units: p value				
number (not applicable)	142	142		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: February the 17th 2017 to February the 1st 2020	
Assessment type	Systematic
Dictionary used	
Dictionary name	non specified
Dictionary version	x
Reporting groups	
Reporting group title	Study population
Reporting group description: Study population (n=142): baseline to month 24	

Serious adverse events	Study population		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 142 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Study population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	68 / 142 (47.89%)		
Cardiac disorders			
Arrhythmia, acute myocardial infarction, hypertension	Additional description: Arrhythmia, acute myocardial infarction, hypertension		
subjects affected / exposed	10 / 142 (7.04%)		
occurrences (all)	10		
Eye disorders			
Cataract, glaucoma	Additional description: Cataract, glaucoma		
subjects affected / exposed	9 / 142 (6.34%)		
occurrences (all)	9		
Respiratory, thoracic and mediastinal disorders			
Upper and lower respiratory tract infection, pneumonia, bronchitis	Additional description: Upper and lower respiratory tract infection, pneumonia, bronchitis		

subjects affected / exposed	10 / 142 (7.04%)		
occurrences (all)	10		
Renal and urinary disorders			
Lower urinary symptoms, infection and kidney stones	Additional description: Lower urinary symptoms, infection and kidney stones		
subjects affected / exposed	9 / 142 (6.34%)		
occurrences (all)	9		
Musculoskeletal and connective tissue disorders			
Fracture	Additional description: Fracture		
subjects affected / exposed	15 / 142 (10.56%)		
occurrences (all)	15		
Arthralgia, osteoarthritis, back pain	Additional description: Arthralgia, osteoarthritis, back pain		
subjects affected / exposed	15 / 142 (10.56%)		
occurrences (all)	15		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 December 2018	We extended the trial with an additional year

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported