



Clinical trial results:

ALOSTRA

Alendronate treatment of osteoporosis in rheumatoid arthritis – indication and duration. A randomized, doubleblind, placebocontrolled multi-centre study to evaluate the effects of discontinuation of alendronate in patients with both rheumatoid arthritis and low bone mass.

Summary

EudraCT number	2015-003638-28
Trial protocol	DK
Global end of trial date	20 December 2021

Results information

Result version number	v1 (current)
This version publication date	12 April 2026
First version publication date	12 April 2026

Trial information

Trial identification

Sponsor protocol code	2015/576
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02944799
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Palle Juul Jensens Boulevard 99, Aarhus N, Denmark,
Public contact	Reumatologisk Forskning, Aarhus University Hospital, anebnie@rm.dk
Scientific contact	Reumatologisk Forskning, Aarhus University Hospital, anebnie@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	04 April 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 January 2021
Global end of trial reached?	Yes
Global end of trial date	20 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of discontinuation of alendronate on bone metabolism in patients with non-glucocorticoid treated rheumatoid arthritis and alendronate-treated osteoporosis with a current T-score in the range of osteopenia.

- to assess the effect of discontinuation of ALN on C-terminal telopeptide crosslinks (CTX) and Type 1 procollagen amino-terminal-propeptide (P1NP) after 6 months
- to assess the effect of discontinuation of ALN on BMD at 2 years

Protection of trial subjects:

All routine biochemical markers (visit 1-5) were analyzed and evaluated promptly. An increase in bone-specific alkaline phosphatase of more than 100% lead to the participant being called in for an extra visit for further evaluation of the cause. The patient was withdrawn from the study if there is suspicion of accelerated bone loss.

All fractures were recorded and in the case of low-energy fracture the patient was withdrawn from the study.

The 12 month DXA scans was reviewed and a BMD decrease of more than 5% lead to exclusion from the study.

Adverse events of special interest included all fractures, and diseases of the upper gastrointestinal tract. All patient-reported adverse events were recorded in a special file in the CRF and the electronic patient record (source data) and evaluated by a study investigator. Investigators immediately reported all SAEs to sponsor. Investigator then provided a detailed report in writing and the study participant in concern was identified with a personal number. Annual reports of all possible adverse events were reported to the Danish Health and Medicines Authority (Sundhedsstyrelsen) in the form of a Development Safety Update Report (DSUR).

Any suspected unsuspected serious adverse events (SUSAR's) were immediately reported by the investigators to Sponsor Ellen-Margrethe Hauge. Sponsor was responsible for reporting all SUSAR's that are life-threatening or result in death to the Danish Health and Medicines Authority (Sundhedsstyrelsen) within 7 days. Within 8 days sponsor reported all relevant information regarding follow-up on the SUSAR. All other SUSARs were reported to the Danish Health and Medicines Authority (Sundhedsstyrelsen) and National Ethics Committee within 15 calendar days by sponsor. All reports of SUSARs included comments on consequences for the trial, if any.

Background therapy:

Patients included in this trial will be treated according to the national Danish guidelines for treatment of RA. In the case of joint swelling the patient were offered a joint injection with GC in the form of triamcinolone acetate, 40 mg/ml. If more than one swollen joint, a maximum of four joints was injected, or a maximum of 4 ml.

Calcium and vitamin D supplement was prescribed in the form of an over-the-counter combination pill (Unikalk Forte) taken twice a day. Each pill contains 100mg calcium carbonate, equivalent to 400mg calcium, and 19µg cholecalciferol, equivalent to 760 international units of vitamin D (IU).

Evidence for comparator: -

Actual start date of recruitment	02 November 2015
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: 50
Worldwide total number of subjects	50
EEA total number of subjects	50

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	30
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

November 2015 - december 2019. Denmark.

Pre-assignment

Screening details:

Participants with RA and low bone mass were recruited both directly from the rheumatology outpatient clinics, as well as by way of an information letter, which was sent to a population of 5000 potential participants who were registered in the National Patient Registry as having RA as well as osteoporosis or osteopenia, but no previous fractures.

Period 1

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

Blinding implementation details:

All patients and investigators were blinded to treatment assignment. The allocation sequence was concealed from the researchers enrolling and assessing participants: The pharmacy provided placebo and ALN tablets in identical grey gelatinous coating in identical packages. Individual non-translucent envelopes marked with each randomization number were provided to each trial site to ensure possibility of individual un-blinding.

Arms

Are arms mutually exclusive?	Yes
Arm title	Withdrawal

Arm description:

Participants randomized to discontinuation of alendronate treatment. Participants instead received placebo tablets.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Placebo tablets
Pharmaceutical forms	Capsule, soft + tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet each week, consisting of: Lactose mono hydrat: 85 mg, Potato starch: 86 mg, Gelatin: 3 mg, Magnesium stearate: 0,9 mg, Tale: 8,1 mg. All specified Ph.Eur, Class C

Arm title	Alendronate
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Arm description:

Continued treatment with alendronate 70 mg weekly

Arm type	Active comparator
Investigational medicinal product name	Alendronate Sodium Monohydrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft + tablet
Routes of administration	Oral use

Dosage and administration details:

alendronate 70 mg tabelt orally once weekly

Number of subjects in period 1	Withdrawal	Alendronate
Started	23	27
6 months assessment	22	24
Completed	14	16
Not completed	9	11
Consent withdrawn by subject	1	2
Adverse event, non-fatal	8	7
other safety concerns	-	2

Baseline characteristics

Reporting groups

Reporting group title	Withdrawal
Reporting group description: Participants randomized to discontinuation of alendronate treatment. Participants instead received placebo tablets.	
Reporting group title	Alendronate
Reporting group description: Continued treatment with alendronate 70 mg weekly	

Reporting group values	Withdrawal	Alendronate	Total
Number of subjects	23	27	50
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	65.1	69.9	
standard deviation	± 7.3	± 8	-
Gender categorical Units: Subjects			
Female	18	21	39
Male	5	6	11
Post-menopausal women			
Number and percentage of participating women who reported as post-menopausal			
Units: Subjects			
yes	18	21	39
no	0	0	0
men	5	6	11
Previous fragility fractures Units: Subjects			
yes	1	3	4
no	22	24	46
Family history of osteoporosis Units: Subjects			
yes	9	11	20
no	14	16	30
Alcohol, >7 per week Units: Subjects			

yes	1	11	12
no	22	16	38
Current smoker Units: Subjects			
Yes	7	4	11
no	16	23	39
Treatment with bDMARDs Units: Subjects			
yes	11	14	25
no	12	13	25
Previous GC treatment Units: Subjects			
yes	9	16	25
no	14	11	25
ACPA positive Units: Subjects			
yes	17	18	35
no	6	9	15
RF positive Units: Subjects			
yes	18	16	34
no	5	11	16
Erosive disease Units: Subjects			
yes	18	21	39
no	5	6	11
DAS28CRP <2.6 Units: Subjects			
yes	15	18	33
no	8	9	17
BMI Units: kg/cm2			
arithmetic mean	24.3	24.4	
standard deviation	± 3.6	± 3.9	-
Years since menopause Units: Years			
arithmetic mean	16.3	23.4	
standard deviation	± 7.9	± 11.6	-
RA disease duration Units: Years			
median	14	13.5	
inter-quartile range (Q1-Q3)	10 to 21	6 to 25	-
Years of alendronate treatment Units: Years			
median	7	6	
inter-quartile range (Q1-Q3)	6 to 10	5 to 9	-
DAS28CRP (score 2-10) Units: arbitrary			
arithmetic mean	2.3	2.2	
standard deviation	± 0.9	± 0.9	-
HAQ (score 0-3)			

Units: arbitrary median inter-quartile range (Q1-Q3)	0.5 0.1 to 1.1	0.6 0.0 to 1.3	-
Number of tender joints (0-40) Units: arbitrary median inter-quartile range (Q1-Q3)	0.0 0.0 to 3.0	0.5 0.0 to 2.0	-
Number of swollen joints (0-40) Units: arbitrary median inter-quartile range (Q1-Q3)	0 0 to 0	0 0 to 0	-
CRP Units: µg/L median inter-quartile range (Q1-Q3)	4.0 1.4 to 6.8	2.0 1.0 to 4.0	-
BMD total hip Units: g/cm2 arithmetic mean standard deviation	0.762 ± 0.081	0.747 ± 0.094	-
BMD lumbar spine Units: g/cm2 arithmetic mean standard deviation	0.827 ± 0.100	0.847 ± 0.101	-
CTX Units: µg/L median inter-quartile range (Q1-Q3)	0.22 0.17 to 0.27	0.20 0.17 to 0.23	-
P1NP Units: µg/L median inter-quartile range (Q1-Q3)	40 31 to 46	32 25 to 41	-
HSS Units: arbitrary median inter-quartile range (Q1-Q3)	27 6 to 51	25.5 7.0 to 136.5	-

End points

End points reporting groups

Reporting group title	Withdrawal
Reporting group description: Participants randomized to discontinuation of alendronate treatment. Participants instead received placebo tablets.	
Reporting group title	Alendronate
Reporting group description: Continued treatment with alendronate 70 mg weekly	

Primary: BMD lumbar spine

End point title	BMD lumbar spine
End point description: Change in BMD of the lumbar spine from baseline to 24 months	
End point type	Primary
End point timeframe: 24 months	

End point values	Withdrawal	Alendronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	27		
Units: g/cm ²				
arithmetic mean (standard deviation)	-0.010 (± 0.007)	0.027 (± 0.006)		

Statistical analyses

Statistical analysis title	Difference between groups
Comparison groups	Withdrawal v Alendronate
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Median difference (final values)
Point estimate	-0.037
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	-0.02

Primary: CTX

End point title	CTX
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End point description:

Change in CTX from baseline to 6 months

End point type	Primary
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End point timeframe:

6 months

End point values	Withdrawal	Alendronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	27		
Units: µg/L				
arithmetic mean (standard deviation)	0.05 (± 0.02)	-0.01 (± 0.02)		

Statistical analyses

Statistical analysis title	Difference between groups
Comparison groups	Withdrawal v Alendronate
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0172
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.11

Primary: P1NP

End point title	P1NP
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End point description:

End point type	Primary
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End point timeframe:

6 months

End point values	Withdrawal	Alendronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	27		
Units: µg/L				
arithmetic mean (standard deviation)	9.98 (± 4.38)	-8.95 (± 4.02)		

Statistical analyses

Statistical analysis title	Difference between groups
Comparison groups	Withdrawal v Alendronate
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0003
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	18.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.72
upper limit	29.13

Secondary: BMD total hip

End point title	BMD total hip
End point description:	
End point type	Secondary
End point timeframe:	
24 months	

End point values	Withdrawal	Alendronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	27		
Units: g/cm ²				
arithmetic mean (standard deviation)	-0.012 (± 0.006)	0.001 (± 0.005)		

Statistical analyses

Statistical analysis title	Difference between groups
Comparison groups	Withdrawal v Alendronate
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0547
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.013
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0

Secondary: BMD lumbar spine

End point title	BMD lumbar spine
End point description:	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Withdrawal	Alendronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	27		
Units: g/cm ²				
arithmetic mean (standard deviation)	-0.012 (± 0.006)	0.001 (± 0.005)		

Statistical analyses

Statistical analysis title	Difference between groups
Comparison groups	Withdrawal v Alendronate

Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0547
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.013
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0

Secondary: BMD total hip

End point title	BMD total hip
End point description:	
End point type	Secondary
End point timeframe:	
12 months	

End point values	Withdrawal	Alendronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	27		
Units: g/cm2				
arithmetic mean (standard deviation)	-0.012 (± 0.06)	0.002 (± 0.005)		

Statistical analyses

Statistical analysis title	Difference between groups
Comparison groups	Withdrawal v Alendronate
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.034
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.015
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0

Secondary: CTX

End point title	CTX
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End point description:

End point type	Secondary
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End point timeframe:

24 months

End point values	Withdrawal	Alendronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	27		
Units: µg/L				
arithmetic mean (standard deviation)	0.02 (± 0.02)	0.00 (± 0.02)		

Statistical analyses

Statistical analysis title	Difference between groups
Comparison groups	Withdrawal v Alendronate
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.5481
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.08

Secondary: P1NP

End point title	P1NP
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End point description:

End point type	Secondary
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End point timeframe:

24 months

End point values	Withdrawal	Alendronate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	27		
Units: µg/L				
arithmetic mean (standard deviation)	12.23 (± 5.48)	-6.71 (± 5.24)		

Statistical analyses

Statistical analysis title	Difference between groups
Comparison groups	Withdrawal v Alendronate
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0069
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	18.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.28
upper limit	32.6

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were assessed at baseline, and at study visits at 3,6,12 and 24 months.

Adverse event reporting additional description:

All patient-reported adverse events were recorded in a special file in the CRF and the electronic patient record (source data) and evaluated by a study investigator.

Assessment type	Systematic
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Dictionary used

Dictionary name	None
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Dictionary version	0
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Reporting groups

Reporting group title	Withdrawal
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Reporting group description:

Participants randomized to discontinuation of alendronate treatment. Participants instead received placebo tablets.

Reporting group title	Alendronate
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Reporting group description:

Continued treatment with alendronate 70 mg weekly

Serious adverse events	Withdrawal	Alendronate	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 23 (39.13%)	11 / 27 (40.74%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignancies			
subjects affected / exposed	2 / 23 (8.70%)	4 / 27 (14.81%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
loss of BMD >5%			
subjects affected / exposed ^[1]	6 / 21 (28.57%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	6 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Other fractures			

subjects affected / exposed	0 / 23 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: Some patients withdrew from the study before assessment of BMD loss >5%, hence they were not exposed to the assessment.

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

Non-serious adverse events	Withdrawal	Alendronate	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)	2 / 27 (7.41%)	
Gastrointestinal disorders			
Upper GI diseases			
subjects affected / exposed	0 / 23 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 June 2018	In protocol version 2.0, the inclusion criterion "Diagnosed with osteoporosis with BMD less than or equal to -2.5 at the hip and/or the lumbar spine" was removed. However, ultimately no patients were included that did not fulfill the criteria of osteoporosis diagnosed by DXA less than or equal to -2.5 at the hip and/or the lumbar spine.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported