Clinical trial results:
The effect of effervescent and buffered alendronate on bone turnover compared to conventional alendronate: A randomized non-inferiority trial

Summary

EudraCT number	2020-005040-35
Trial protocol	DK
Global end of trial date	24 August 2022

Results information

Result version number	v1 (current)
This version publication date	05 July 2023
First version publication date	05 July 2023

Trial information

Trial identification

Sponsor protocol code	0120

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05325515
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Palle Juul-Jensens Boulevard 99, Aarhus N, Denmark, 8200
Public contact	Dept. of Endocrinology , Aarhus University Hospital, +45 78455470, torbhars@rm.dk
Scientific contact	Dept. of Endocrinology , Aarhus University Hospital, +45 78455470, torbhars@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	01 December 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 August 2022
Global end of trial reached?	Yes
Global end of trial date	24 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate if Binosto decreases bone resorption to the same extent as Fosamax

Protection of trial subjects:

The study was monitored by the GCP-unit at Aarhus University, Denmark

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 64
Worldwide total number of subjects	64
EEA total number of subjects	64

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)	30
From 65 to 84 years	34
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were identified at the Osteoporosis Clinic, Aarhus University Hospital, Denmark. Postmenopausal women with BMD T-score were invited by letter for further participation.

Pre-assignment

Screening details:

We screened 96 individuals for inclusion. 2 of those withdrew consent and 30 were excluded due to exclusion criteria. Thus we ended up with 64 participants that we randomized 1:1.

Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Binosto

Arm description:

Experimental treatment with effervescent and buffered alendronate

Arm type	Experimental
Investigational medicinal product name	Binosto
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Effervescent tablet
Routes of administration	Oral use

Dosage and administration details:

70mg in one tablet weekly

Arm title	Fosamax

Arm description:

Active comparator

Arm type	Active comparator
Investigational medicinal product name	Fosamax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

70 mg in one tablet weekly

Number of subjects in period 1	Binosto	Fosamax
Started	32	32
Completed	29	27
Not completed	3	5
Consent withdrawn by subject	1	1
Adverse event, non-fatal	1	4
Serious adverse event, unrelated	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Binosto
Reporting group description:	
Experimental treatment with effervescent and buffered alendronate	
Reporting group title	Fosamax
Reporting group description:	
Active comparator	

Reporting group values	Binosto	Fosamax	Total
Number of subjects	32	32	64
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	20	21	41
From 65-84 years	12	11	23
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	61.9	61.8	
standard deviation	± 6	± 6.2	-
Gender categorical			
Units: Subjects			
Female	32	32	64
Years since menopause			
Units: years			
arithmetic mean	11.9	14.0	
standard deviation	± 5.7	± 6.2	-
Lumbar spine T-score			
Units: None			
arithmetic mean	-1.9	-1.7	
standard deviation	± 0.8	± 0.6	-
Total hip T-score			
Units: None			
arithmetic mean	-1.5	-1.4	
standard deviation	± 0.6	± 0.6	-
Femoral neck T-score			
Units: None			
arithmetic mean	-1.8	-1.8	
standard deviation	± 0.6	± 0.5	-
CTx			

Units: microgram(s)/litre			
median	0.6	0.6	
full range (min-max)	0.43 to 1.07	0.43 to 1.16	-

End points

End points reporting groups	
Reporting group title	Binosto
Reporting group description: Experimental treatment with effervescent and buffered alendronate	
Reporting group title	Fosamax
Reporting group description: Active comparator	

Primary: Decrease in bone resorption

End point title	Decrease in bone resorption
End point description:	
End point type	Primary
End point timeframe: Baseline to week 16	

End point values	Binosto	Fosamax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	27		
Units: percent				
arithmetic mean (standard deviation)	-47 (± 23)	-58 (± 24)		

Statistical analyses

Statistical analysis title	Primary end point
Statistical analysis description: We analyzed if the decrease in bone resorption with Binosto was non-inferior to that with Fosamax	
Comparison groups	Binosto v Fosamax
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.05
Method	Comparison of means and CIs

Notes:
[1] - The non-inferiority test came out indeterminate

Secondary: Decrease in bone formation

End point title	Decrease in bone formation
End point description:	

End point type	Secondary

End point timeframe:
Baseline to week 16

End point values	Binosto	Fosamax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	27		
Units: percent				
arithmetic mean (standard deviation)	-35 (± 21)	-46 (± 23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Persistence

End point title	Persistence

End point description:

End point type	Secondary

End point timeframe:
Baseline to week 16

End point values	Binosto	Fosamax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	27		
Units: Percent	100	96		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Baseline to 16 weeks	
Assessment type	Systematic
Dictionary used	
Dictionary name	SNOMED CT
Dictionary version	aug 22
Reporting groups	
Reporting group title	BINOSTO
Reporting group description: -	
Reporting group title	FOSAMAX
Reporting group description: -	

Serious adverse events	BINOSTO	FOSAMAX	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Reproductive system and breast disorders			
Breast cancer			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	BINOSTO	FOSAMAX	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 32 (56.25%)	17 / 32 (53.13%)	
General disorders and administration site conditions			
Headache			
subjects affected / exposed	2 / 32 (6.25%)	3 / 32 (9.38%)	
occurrences (all)	2	3	
Fracture			

subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 32 (12.50%)	3 / 32 (9.38%)	
occurrences (all)	4	3	
Diarrhoea			
subjects affected / exposed	9 / 32 (28.13%)	5 / 32 (15.63%)	
occurrences (all)	9	5	
Reflux gastritis			
subjects affected / exposed	2 / 32 (6.25%)	5 / 32 (15.63%)	
occurrences (all)	2	5	

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