



## 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     |
| <b>Arm title</b>             | 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

|                  |         |
|------------------|---------|
| <b>Arm title</b> | 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

| <b>Number of subjects in period 1</b> | 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 <sup>[1]</sup> |
| 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<br>occurrences (all) | 1 / 32 (3.13%)<br>1 | 1 / 32 (3.13%)<br>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

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported