Clinical trial results:
A Multinational, Randomized, Double-Blind, Active-Controlled Phase 3 Study to Compare the Clinical Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of EB1001 Biosimilar With EU-Licensed Prolia® in Postmenopausal Women With Osteoporosis

Summary

EudraCT number	2021-002187-49
Trial protocol	HU EE BG
Global end of trial date	28 July 2023

Results information

Result version number	v1 (current)
This version publication date	06 April 2025
First version publication date	06 April 2025

Trial information

Trial identification

Sponsor protocol code	EB-CLIN-1001-03

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Eden Biologics, Inc.
Sponsor organisation address	5F. No. 18, Sec 2., Shengyi Rd. Zhubei City, Hsinchu County 302, Zhubei, Taiwan,
Public contact	Stephen B. Shrewsbury, Eden Biologics, Inc., +1415 2501169, sshrewsbury@edenbiologics.com
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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	12 February 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 July 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

- To demonstrate the equivalence between EB1001 and EU-licensed Prolia in terms of change in bone marrow density (BMD) at the lumbar spine from baseline to Month 12 in postmenopausal women with osteoporosis.
- To demonstrate the pharmacodynamic similarity between EB1001 and EU-licensed Prolia for the area under the effect curve (AUEC) of s-CTX (serum carboxy-terminal cross-linking telopeptide of type I collagen) from baseline to Month 6 in postmenopausal women with osteoporosis.

Protection of trial subjects:

The study was conducted accordance with the ethical principles that have their origin in the Declaration of Helsinki, ICH GCP, and all applicable regulations.

Background therapy:

Calcium and vitamin D were co-administered to prevent low serum calcium level while taking study drugs. All patients were to receive daily supplementation containing 1000 mg of elemental calcium and 400 IU vitamin D from randomization until the EoS visit (Month 12).

Evidence for comparator:

The EU-Licensed Prolia® is used as active comparator.

Actual start date of recruitment	24 September 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	Poland: 52
Country: Number of subjects enrolled	Estonia: 9
Worldwide total number of subjects	61
EEA total number of subjects	61

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)	19
From 65 to 84 years	42
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 203 patients were screened for the study. Of these, a total of 61 patients were randomly assigned - 29 patients in EB1001 group and 32 in EU-licensed Prolia group. All patients in EB1001 group and 30 patients in EU-licensed Prolia group completed the study treatment. 2 patients in EU-licensed Prolia group discontinued the study treatment

Pre-assignment

Screening details:

The study comprised of screening evaluations which were to be completed within 28 days prior to randomization. After the screening period, patients were to undergo 12-months treatment period. Eligible patients were to be randomized (1:1) to receive either EB1001(60 mg) or EU-licensed Prolia (60 mg) via SC injection on Day 1 and at Month 6.

Period 1

Period 1 title	Treatment period (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:

Treatment period was double-blinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	EB1001 Group

Arm description:

EB1001 60 mg on Day 1 and Month 6

Arm type	Experimental
Investigational medicinal product name	EB1001
Investigational medicinal product code	
Other name	JHL1266
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

EB1001 (60 mg) was administered using a PFS of 60 mg/1 mL solution on Day 1 (Week 0, the same date as randomization) and at Month 6. The EoS visit was to occur at Month 12.

Arm title	EU-licensed Prolia Group

Arm description:

Prolia 60 mg on Day 1 and Month 6

Arm type	Active comparator
Investigational medicinal product name	EU-licensed Prolia
Investigational medicinal product code	
Other name	Denosumab
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

EU-licensed Prolia (60 mg) was administered using a PFS of 60 mg/1 mL solution on Day 1 (Week 0, the same date as randomization) and at Month 6. The EoS visit was to occur at Month 12.

Number of subjects in period 1	EB1001 Group	EU-licensed Prolia Group
Started	29	32
Completed	29	30
Not completed	0	2
Consent withdrawn by subject	-	1
Adverse event, non-fatal	-	1

Baseline characteristics

Reporting groups	
Reporting group title	EB1001 Group
Reporting group description: EB1001 60 mg on Day 1 and Month 6	
Reporting group title	EU-licensed Prolia Group
Reporting group description: Prolia 60 mg on Day 1 and Month 6	

Reporting group values	EB1001 Group	EU-licensed Prolia Group	Total
Number of subjects	29	32	61
Age categorical Units: Subjects			
Adults (18-64 years)	8	11	19
From 65-84 years	21	21	42
Gender categorical Units: Subjects			
Female	29	32	61
Male	0	0	0

End points

End points reporting groups

Reporting group title	EB1001 Group
Reporting group description: EB1001 60 mg on Day 1 and Month 6	
Reporting group title	EU-licensed Prolia Group
Reporting group description: Prolia 60 mg on Day 1 and Month 6	

Primary: Primary Efficacy Endpoint: Percent change in BMD at the lumbar spine (L1 to L4) by DXA from baseline to Month 12

End point title	Primary Efficacy Endpoint: Percent change in BMD at the lumbar spine (L1 to L4) by DXA from baseline to Month 12[1]
End point description: The "0" in the below table is dummy value - not result.	
End point type	Primary
End point timeframe: Due to the early termination of this study, the primary efficacy endpoint was not evaluated in the study.	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the early termination of this study, the primary efficacy endpoint was not evaluated in the study and, therefore no statistical analyses for this primary end point.

End point values	EB1001 Group	EU-licensed Prolia Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	32		
Units: percent				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Primary PD Endpoint: The AUEC of s-CTX from Day 1 predose to Month 6 predose

End point title	Primary PD Endpoint: The AUEC of s-CTX from Day 1 predose to Month 6 predose[2]
End point description: The "0" in the below table is dummy value - not result.	
End point type	Primary
End point timeframe: Due to the early termination of this study, the primary PD endpoint was not evaluated in the study.	

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the early termination of this study, the primary efficacy endpoint was not evaluated in the study and, therefore no statistical analyses for this primary end point.

End point values	EB1001 Group	EU-licensed Prolia Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	32		
Units: percent				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety Endpoints

End point title	Safety Endpoints

End point description:

All safety analyses were conducted on the Safety Set (patients received 1 full or partial dose). All summary tables were based on TEAEs. No clinical safety labs, vital signs, ECG, or physical examination endpoints were derived for the final analysis.

End point type	Secondary

End point timeframe:

During study treatment

End point values	EB1001 Group	EU-licensed Prolia Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	32		
Units: Number of Patients with				
Any TEAE	15	15		
Any Serious TEAE	1	1		
Any Grade 3 or Higher TEAE	2	1		
Any Treatment-related TEAE	10	7		
Any AESI	6	12		
Any TEAE Leading to Treatment Discontinuation	0	1		
Any TEAE Leading to Study Discontinuation	0	1		
Any TEAE Leading to Death	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Local Injection Site Pain (Visual Analogue Scale)

End point title	Local Injection Site Pain (Visual Analogue Scale)

End point description:

Local injection site pain (visual analogue scale) was analysed in the Safety Set (patients received 1 full or partial dose).

End point type	Secondary

End point timeframe:

On Baseline and Day 183

End point values	EB1001 Group	EU-licensed Prolia Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	32		
Units: millimeter				
arithmetic mean (standard deviation)				
Visual Analogue Scale (mm) - Baseline	1.1 (± 2.28)	1.0 (± 2.53)		
Visual Analogue Scale (mm) - Day 183	4.6 (± 11.81)	1.9 (± 3.79)		
Visual Analogue Scale (mm) - Change from Baseline	3.5 (± 10.79)	0.9 (± 4.49)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All safety analyses were conducted on the Safety Set during the treatment period. The Safety Set was defined as all randomly assigned patients who receive at least 1 dose (full or partial) of the study drug (EB1001 or EU-licensed Prolia).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	EB1001
Reporting group description: -	
Reporting group title	EU-licensed Prolia

Reporting group description: -

Serious adverse events	EB1001	EU-licensed Prolia	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 29 (3.45%)	1 / 32 (3.13%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	1 / 29 (3.45%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 29 (3.45%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 29 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	0 / 29 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration			
subjects affected / exposed	0 / 29 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspirin-exacerbated respiratory disease			
subjects affected / exposed	0 / 29 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	EB1001	EU-licensed Prolia	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 29 (48.28%)	12 / 32 (37.50%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 29 (10.34%)	0 / 32 (0.00%)	
occurrences (all)	3	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 29 (6.90%)	0 / 32 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Sciatica			
subjects affected / exposed	2 / 29 (6.90%)	0 / 32 (0.00%)	
occurrences (all)	2	0	
Endocrine disorders			

Hypothyroidism			
subjects affected / exposed	2 / 29 (6.90%)	0 / 32 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 29 (6.90%)	0 / 32 (0.00%)	
occurrences (all)	2	0	
Muscle spasms			
subjects affected / exposed	2 / 29 (6.90%)	0 / 32 (0.00%)	
occurrences (all)	2	0	
Back pain			
subjects affected / exposed	0 / 29 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 29 (6.90%)	0 / 32 (0.00%)	
occurrences (all)	2	0	
COVID-19			
subjects affected / exposed	0 / 29 (0.00%)	3 / 32 (9.38%)	
occurrences (all)	0	3	
Upper respiratory tract infection			
subjects affected / exposed	0 / 29 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	
Urinary tract infection			
subjects affected / exposed	0 / 29 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	0 / 29 (0.00%)	3 / 32 (9.38%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 May 2021	Protocol Version 1.0 dated 24 May 2021 - Original protocol
22 July 2021	Protocol Version 2.0 dated 22 Jul 2021 - Amendment 1 The amendment is considered minor because it does not significantly impact the safety or physical/mental integrity of participants. No patients have been enrolled as of the date of this amendment. Per the recommendations of Committee for Medicinal Products for Human Use (CHMP) regarding the overall study design, a restricted weight range of 50 to 100 kg for study participants is endorsed, as this would increase homogeneity of the participant population. To address this recommendation, inclusion criterion #4 concerning a body weight range has been added in Section 4.1.1 Inclusion Criteria: ''Inserted inclusion criterion #4 "Body weight between 40.0 and 99.9 kg, both inclusive, when rounded to the nearest tenth."

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported