Clinical trial results:
Denosumab in the prevention of immobilization-induced bone loss in Intensive Care Unit patients

Summary

EudraCT number	2018-000552-18
Trial protocol	AT
Global end of trial date	24 March 2022

Results information

Result version number	v1 (current)
This version publication date	09 March 2024
First version publication date	09 March 2024

Trial information

Trial identification

Sponsor protocol code	1155/2018

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University of Vienna
Sponsor organisation address	Waehringer Guertel 18-20, Vienna, Austria, 1090
Public contact	Clincial Trial Information Desk, Medical University of Vienna, 0043 14040043330, pmr-office@meduniwien.ac.at
Scientific contact	Clincial Trial Information Desk, Medical University of Vienna, 0043 14040043330, pmr-office@meduniwien.ac.at

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	24 March 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 March 2022
Global end of trial reached?	Yes
Global end of trial date	24 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

twofold:
a) to evaluate if a single administration of denosumab decreases bone resorption (CTX-1) within one month in immobilized patients
b) to evaluate if one year of denosumab therapy has a positive effect on the immobilization-associated bone loss. (hip region) Additionally, potential changes of BTMs will be evaluated.

Pilot study (n=14):
evaluate if a single administration of denosumab decreases bone resorption (CTX-1) within one month in immobilized patients

Protection of trial subjects:

Trial subjects were protected by periodic follow up appointments after study inclusion.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 December 2019
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	Austria: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

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)	12

From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

patients with acute aSAH HH IV/V or ICH and severe neurological deficits, reduced state of consciousness, age 30-80, excl: intake of drugs with potential effects on BMD, fragility fracture within the previous six months, non-osteoporotic bone disease, severe renal insufficiency, malignant disease in the preceding five years, pregnancy, DM

Period 1

Period 1 title	Baseline Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Denosumab

Arm description:

Within 72 hours after ICU admission, they were randomized in a 1:1 ratio to receive denosumab 60 mg subcutaneously.

Arm type	Experimental
Investigational medicinal product name	Denosumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Within 72 hours after ICU admission, they were randomized in a 1:1 ratio to receive denosumab 60 mg subcutaneously.

Arm title	Placebo

Arm description:

Within 72 hours after ICU admission, they were randomized in a 1:1 ratio to receive placebo subcutaneously.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Within 72 hours after ICU admission, they were randomized in a 1:1 ratio to receive placebo subcutaneously.

Number of subjects in period 1	Denosumab	Placebo
Started	7	7
Completed	7	7

Baseline characteristics

End points

End points reporting groups

Reporting group title	Denosumab
Reporting group description:	
Within 72 hours after ICU admission, they were randomized in a 1:1 ratio to receive denosumab 60 mg subcutaneously.	
Reporting group title	Placebo
Reporting group description:	
Within 72 hours after ICU admission, they were randomized in a 1:1 ratio to receive placebo subcutaneously.	

Primary: CTX 1

End point title	CTX 1
End point description:	
End point type	Primary
End point timeframe:	
The primary endpoint was group differences in the percentage change of C-terminal telopeptide of type 1 collagen (CTX-1) levels in serum from denosumab/placebo application to four weeks thereafter.	

End point values	Denosumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	7		
Units: ng/ml				
number (not applicable)	7	7		

Statistical analyses

Statistical analysis title	Primary endpoint
Statistical analysis description:	
The pre-specified primary endpoint was the percentage change in serum levels of C-terminal telopeptide of type 1 collagen (CTX-1) from the time of denosumab/placebo application to four weeks thereafter.	
Comparison groups	Denosumab v Placebo
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05 [1]
Method	ANCOVA

Notes:

[1] - Statistical analysis was performed using SAS 9.4 based on a two-sided significance level of 5%.

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

6 months after study inclusion. No adverse events related to the study medication were observed during the first 4 weeks after application as well as during the follow-up period. Serum calcium levels remained within the normal range.

Assessment type	Systematic

Dictionary used

Dictionary name	SNOMED CT
Dictionary version	1

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No adverse events related to the study medication were observed during the first four weeks after application as well as during the follow-up period. Serum calcium levels remained within the normal range. One patient died within four weeks after aSAH due to fatal general brain edema based on previous vasospasm and cerebral infarction. The patient never received denosumab because she was in the placebo group.

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/36056473