Clinical trial results:
RANKL-blockade for the treatment of erosive osteoarthritis (OA) of interphalangeal finger joints

Randomized, double blind, placebo-controlled study to evaluate the efficacy of denosumab 60mg sc every 3 months in patients with erosive osteoarthritis of the interphalangeal finger joints

Summary

EudraCT number	2015-003223-53
Trial protocol	BE
Global end of trial date	28 April 2021

Results information

Result version number	v1 (current)
This version publication date	08 August 2024
First version publication date	08 August 2024
Summary attachment (see zip file)	Final Study Report (2015-003223-53_Denosumab_Final study report_2022-04-11.pdf)

Trial information

Trial identification

Sponsor protocol code	AGO/2015/008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01575873
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UZ Gent
Sponsor organisation address	Corneel Heymanslaan 10, Gent, Belgium, 9000
Public contact	Bimetra Clinics, Ghent University Hospital, +32 93320500, bimetra.clinics@uzgent.be
Scientific contact	Bimetra Clinics, Ghent University Hospital, +32 93320500, bimetra.clinics@uzgent.be

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	11 April 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of denosumab on the reduction of radiographic erosive progression using GUSS™ (Ghent University Score System).

Protection of trial subjects:

Ethics review and approval, informed consent, supportive care and routine monitoring.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 March 2016
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	Belgium: 100
Worldwide total number of subjects	100
EEA total number of subjects	100

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)	60
From 65 to 84 years	40
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

136 patients were screened in the period from 30/03/2016 till 04/07/2018. 100 patients were included, 100 patients were randomised. 87 patients were included and completed the trial. End of trial notification was dated 28/04/2021 (last patient last visit) and submitted to EC and CA 25/05/2021

Pre-assignment

Screening details:

Main in- and exclusioncriteria

Period 1

Period 1 title	Placebo controlled phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	patients allocated to placebo

Arm description:

Patients received every 3 months placebo for denosumab in identical containers and stored/packaged the same as drug product denosumab.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo for Denosumab will be presented in identical containers and stored/packaged the same as drug product denosumab.

Arm title	patient allocated to denosumab

Arm description:

Patients were treated with blinded study medication containing 60 mg denosimab subcutaneously every 3 months.

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

Dosage and administration details:

The study drug used in this arm is denosumab 60 mg subcutaneously every 3 months. It was provided as sterile, solution for injection in 1 ml pre-filled syringes containing denosumab 60mg/ ml

Number of subjects in period 1	patients allocated to placebo	patient allocated to denosumab
Started	49	51
Completed	46	46
Not completed	3	5
Consent withdrawn by subject	-	1
Adverse event, non-fatal	3	3
Protocol deviation	-	1

Period 2

Period 2 title	Open label phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Open label arm

Arm description:

All patients were treated with denosumab 60mg subcutaneous every 3 months

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

Dosage and administration details:

The study drug used in open label phase is denosumab 60 mg subcutaneously every 3 months. It will be provided as sterile, solution for injection in 1 ml pre-filled syringes containing denosumab 60mg/ ml

Number of subjects in period 2	Open label arm
Started	92
Completed	87
Not completed	5
Consent withdrawn by subject	5

Baseline characteristics

End points

End points reporting groups

Reporting group title	patients allocated to placebo
Reporting group description:	
Patients received every 3 months placebo for denosumab in identical containers and stored/packaged the same as drug product denosumab.	
Reporting group title	patient allocated to denosumab
Reporting group description:	
Patients were treated with blinded study medication containing 60 mg denosimab subcutaneously every 3 months.	
Reporting group title	Open label arm
Reporting group description:	
All patients were treated with denosumab 60mg subcutaneous every 3 months	

Primary: Primary radiographic efficacy endpoint

End point title	Primary radiographic efficacy endpoint
End point description:	
End point type	Primary
End point timeframe:	
Change in total GUSS in the denosumab group compared to the placebo group at week 24.	

End point values	patients allocated to placebo	patient allocated to denosumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	51		
Units: Incidence of new erosive joints				
number (not applicable)	5.1	2.3		

Statistical analyses

Statistical analysis title	ITT approach on the FAS population
Statistical analysis description:	
Changes in GUSS (Ghent University Score System) will be analyzed at joint level with generalized estimating equations (GEE), accounting for within-patient clustering. Robust standard errors will be used and the working correlation structure specified exchangeable. Data from baseline, week 12 and week 24 will be used. The independent variables included in the model are treatment group, visit number, interaction between treatment group and visit number, and the baseline value of dependent variable	
Comparison groups	patients allocated to placebo v patient allocated to denosumab

Number of subjects included in analysis	100
Analysis specification	Post-hoc
Analysis type	superiority
P-value	< 0.05 [1]
Method	t-test, 2-sided

Notes:

[1] - Allefficacy analyses will be presented by a point estimate of the difference between the treatment groups, with a 95% confidence interval (95%CI) and the two-sided p-value. A p-value below 0.05 (p<0.05) will be considered statistically significant.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported between the first dose administration of trial medication and the last trial related activity.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25

Reporting groups

Reporting group title	patients allocated to placebo
Reporting group description: -	
Reporting group title	patients allocated to denosumab
Reporting group description: -	
Reporting group title	Open label group

Reporting group description: -

Serious adverse events	patients allocated to placebo	patients allocated to denosumab	Open label group
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 49 (12.24%)	5 / 51 (9.80%)	9 / 92 (9.78%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer			
subjects affected / exposed	3 / 49 (6.12%)	0 / 51 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute Coronary Syndrome			
subjects affected / exposed	0 / 49 (0.00%)	1 / 51 (1.96%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Surgical and medical procedures			
subjects affected / exposed	1 / 49 (2.04%)	3 / 51 (5.88%)	3 / 92 (3.26%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Confusional state			
subjects affected / exposed	0 / 49 (0.00%)	0 / 51 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal disorder			
subjects affected / exposed	0 / 49 (0.00%)	0 / 51 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Cystopexie			
subjects affected / exposed	1 / 49 (2.04%)	0 / 51 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Musculoskeletal complaints			
subjects affected / exposed	1 / 49 (2.04%)	2 / 51 (3.92%)	5 / 92 (5.43%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Infections			
subjects affected / exposed	1 / 49 (2.04%)	1 / 51 (1.96%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	patients allocated to placebo	patients allocated to denosumab	Open label group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 49 (93.88%)	44 / 51 (86.27%)	80 / 92 (86.96%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign melanoma			
subjects affected / exposed	1 / 49 (2.04%)	0 / 51 (0.00%)	0 / 92 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			

Vascular disorders			
subjects affected / exposed	1 / 49 (2.04%)	0 / 51 (0.00%)	4 / 92 (4.35%)
occurrences (all)	1	0	4
Surgical and medical procedures			
Surgical and medical procedures			
subjects affected / exposed	4 / 49 (8.16%)	1 / 51 (1.96%)	5 / 92 (5.43%)
occurrences (all)	4	1	5
Teeth problems			
subjects affected / exposed	4 / 49 (8.16%)	3 / 51 (5.88%)	12 / 92 (13.04%)
occurrences (all)	7	3	16
Immune system disorders			
Immune system disorders			
subjects affected / exposed	1 / 49 (2.04%)	1 / 51 (1.96%)	2 / 92 (2.17%)
occurrences (all)	1	1	2
Reproductive system and breast disorders			
Reproductive system			
subjects affected / exposed	1 / 49 (2.04%)	1 / 51 (1.96%)	1 / 92 (1.09%)
occurrences (all)	1	1	1
Respiratory, thoracic and mediastinal disorders			
Respiratory and thoracic disorders			
subjects affected / exposed	21 / 49 (42.86%)	20 / 51 (39.22%)	27 / 92 (29.35%)
occurrences (all)	30	27	37
Psychiatric disorders			
depression			
subjects affected / exposed	0 / 49 (0.00%)	1 / 51 (1.96%)	1 / 92 (1.09%)
occurrences (all)	0	1	1
Cardiac disorders			
cardiac disorders			
subjects affected / exposed	3 / 49 (6.12%)	1 / 51 (1.96%)	4 / 92 (4.35%)
occurrences (all)	3	1	4
Nervous system disorders			
Nervous system disorder			
subjects affected / exposed	12 / 49 (24.49%)	5 / 51 (9.80%)	6 / 92 (6.52%)
occurrences (all)	18	6	10
Blood and lymphatic system disorders			
Blood and lymphatic system disorders			

subjects affected / exposed	1 / 49 (2.04%)	0 / 51 (0.00%)	5 / 92 (5.43%)
occurrences (all)	4	0	5
Ear and labyrinth disorders			
Ear disorders			
subjects affected / exposed	2 / 49 (4.08%)	2 / 51 (3.92%)	0 / 92 (0.00%)
occurrences (all)	2	2	0
Eye disorders			
Eye disorders			
subjects affected / exposed	3 / 49 (6.12%)	0 / 51 (0.00%)	6 / 92 (6.52%)
occurrences (all)	5	0	9
Gastrointestinal disorders			
Gastrointestinal disorders			
subjects affected / exposed	10 / 49 (20.41%)	12 / 51 (23.53%)	8 / 92 (8.70%)
occurrences (all)	12	14	8
Hepatobiliary disorders			
Hepatobiliary disorders			
subjects affected / exposed	1 / 49 (2.04%)	0 / 51 (0.00%)	5 / 92 (5.43%)
occurrences (all)	1	0	5
Skin and subcutaneous tissue disorders			
Skin and subcutaneous disorders			
subjects affected / exposed	2 / 49 (4.08%)	6 / 51 (11.76%)	8 / 92 (8.70%)
occurrences (all)	3	6	8
Renal and urinary disorders			
Renal and urinary disorders			
subjects affected / exposed	3 / 49 (6.12%)	4 / 51 (7.84%)	5 / 92 (5.43%)
occurrences (all)	9	9	11
Endocrine disorders			
Endocrine disorders			
subjects affected / exposed	0 / 49 (0.00%)	1 / 51 (1.96%)	1 / 92 (1.09%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders			
subjects affected / exposed	22 / 49 (44.90%)	17 / 51 (33.33%)	38 / 92 (41.30%)
occurrences (all)	40	26	55
Infections and infestations			
Infections ans infestations			

subjects affected / exposed occurrences (all)	8 / 49 (16.33%) 8	6 / 51 (11.76%) 7	17 / 92 (18.48%) 17

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 February 2016	This amendment considers an administrative error and is considered to be not substantial. The overall reason for the amendment: The overall reason for the amendment is based upon standard clinical practice and patients' best interest. No new exams will be added only the time points of the exams will be changed.
17 October 2018	The overall reason for the amendment: The overall reason for the amendment is based upon the request for a study extension with another 48 weeks.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported