Clinical trial results:
A Phase 3 Randomized, Double-Blind, Placebo-Controlled, Multicenter Study of The Analgesic Efficacy and Safety of The Subcutaneous Administration of Tanezumab (Pf-04383119) In Subjects With Cancer Pain Predominantly Due to Bone Metastasis Receiving Background Opioid Therapy

Summary

EudraCT number	2013-002223-42
Trial protocol	AT CZ GB PL ES SK HU RO FR DE
Global end of trial date	25 June 2021

Results information

Result version number	v2 (current)
This version publication date	29 December 2022
First version publication date	09 July 2022
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	A4091061

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02609828
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com

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	21 October 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Demonstrate superior analgesic efficacy of tanezumab 20 mg SC versus matching placebo SC at Week 8 in subjects, with cancer pain predominantly due to bone metastasis, receiving background opioid therapy.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 October 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 1
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Brazil: 7
Country: Number of subjects enrolled	Chile: 6
Country: Number of subjects enrolled	China: 17
Country: Number of subjects enrolled	Czechia: 1
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	Japan: 11
Country: Number of subjects enrolled	Korea, Republic of: 7
Country: Number of subjects enrolled	Poland: 50
Country: Number of subjects enrolled	Romania: 22
Country: Number of subjects enrolled	Slovakia: 17
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United Kingdom: 5
Worldwide total number of subjects	155
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)	96
From 65 to 84 years	59
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects with cancer pain mainly due to bone metastasis,receiving background opioid therapy,randomised to 3 treatment arms:tanezumab20milligrams(mg),10mg,placebo. After study start,10mg arm discontinued(protocol amendment3)no new subjects enrolled in this arm. Existing subjects in arm received 20 mg for remaining doses and included in10/20mg arm.

Pre-assignment

Screening details:

Total 325 subjects signed the inform consent form (ICF). Out of which 158 subjects were screen failures, and 11 subjects were screened but not enrolled and randomised into the study. Total of 156 subjects were enrolled and randomised into the study and assigned to study treatments.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received placebo matched to tanezumab subcutaneous (SC) once every 8 weeks for 24 weeks.

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

Dosage and administration details:

Placebo matched to Tanezumab was administered via SC injection once every 8 weeks for 24 weeks. All subjects received 1 mL of study medication administered as a SC injection. Administered in the abdomen or anterior aspect of the thigh.

Arm title	Tanezumab 10 mg

Arm description:

Subjects in this discontinued treatment arm, received tanezumab 10 mg SC once every 8 weeks before protocol amendment 3 and completed their treatment before the amendment.

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

Dosage and administration details:

Subjects received Tanezumab 10 mg/mL, SC once every 8 weeks before protocol amendment 3 and completed their treatment before the amendment. Administered in the abdomen or anterior aspect of the thigh.

Arm title	Tanezumab 10/20 mg

Arm description:

Subjects in this treatment group had received tanezumab 10 mg SC once every 8 weeks before protocol

amendment 3 and after the amendment they continued remaining treatment with tanezumab 20 mg SC once every 8 weeks.

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

Dosage and administration details:

Subjects received tanezumab 10 mg/ml SC, once every 8 weeks before protocol amendment 3 and after the amendment they continued remaining treatment with tanezumab 20 mg SC once every 8 weeks. Administered in the abdomen or anterior aspect of the thigh.

Arm title	Tanezumab 20 mg

Arm description:

Subjects received tanezumab 20 mg SC once every 8 weeks for 24 weeks.

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

Dosage and administration details:

Subjects received tanezumab 20 mg/ml SC once every 8 weeks for 24 weeks. Administered in the abdomen or anterior aspect of the thigh.

Number of subjects in period 1	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg
Started	73	9	1
Treated	73	9	1
Completed	31	5	0
Not completed	42	4	1
Consent withdrawn by subject	12	1	-
Adverse event, non-fatal	8	1	-
Death	15	1	1
Unspecified	3	-	-
Lost to follow-up	-	-	-
Insufficient clinical response	2	1	-
Protocol deviation	2	-	-

Number of subjects in period 1	Tanezumab 20 mg
Started	72
Treated	72
Completed	29
Not completed	43
Consent withdrawn by subject	10
Adverse event, non-fatal	6

Death	19
Unspecified	6
Lost to follow-up	1
Insufficient clinical response	-
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matched to tanezumab subcutaneous (SC) once every 8 weeks for 24 weeks.	
Reporting group title	Tanezumab 10 mg
Reporting group description:	
Subjects in this discontinued treatment arm, received tanezumab 10 mg SC once every 8 weeks before protocol amendment 3 and completed their treatment before the amendment.	
Reporting group title	Tanezumab 10/20 mg
Reporting group description:	
Subjects in this treatment group had received tanezumab 10 mg SC once every 8 weeks before protocol amendment 3 and after the amendment they continued remaining treatment with tanezumab 20 mg SC once every 8 weeks.	
Reporting group title	Tanezumab 20 mg
Reporting group description:	
Subjects received tanezumab 20 mg SC once every 8 weeks for 24 weeks.	

Reporting group values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg
Number of subjects	73	9	1
Age Categorical Units: Subjects			
>=18 to < 45 years	10	1	0
>=45 to <65 years	44	4	1
>=65 years	19	4	0
Age continuous Units: years			
arithmetic mean	58.0	61.6	58.0
standard deviation	± 11.1	± 9.9	± 99999
Sex: Female, Male Units: Subjects			
Female	39	4	0
Male	34	5	1
Race Units: Subjects			
Asian	16	3	0
Black or African American	1	0	0
White	56	6	1
Ethnicity Units: Subjects			
Hispanic or Latino	10	0	0
Not Hispanic or Latino	63	9	1

Reporting group values	Tanezumab 20 mg	Total	
Number of subjects	72	155	
Age Categorical Units: Subjects			
>=18 to < 45 years	3	14	

>=45 to <65 years	33	82	
>=65 years	36	59	

Age continuous Units: years			
arithmetic mean	63.5		
standard deviation	± 10.1	-	
Sex: Female, Male Units: Subjects			
Female	26	69	
Male	46	86	
Race Units: Subjects			
Asian	16	35	
Black or African American	1	2	
White	55	118	
Ethnicity Units: Subjects			
Hispanic or Latino	5	15	
Not Hispanic or Latino	67	140	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matched to tanezumab subcutaneous (SC) once every 8 weeks for 24 weeks.	
Reporting group title	Tanezumab 10 mg
Reporting group description:	
Subjects in this discontinued treatment arm, received tanezumab 10 mg SC once every 8 weeks before protocol amendment 3 and completed their treatment before the amendment.	
Reporting group title	Tanezumab 10/20 mg
Reporting group description:	
Subjects in this treatment group had received tanezumab 10 mg SC once every 8 weeks before protocol amendment 3 and after the amendment they continued remaining treatment with tanezumab 20 mg SC once every 8 weeks.	
Reporting group title	Tanezumab 20 mg
Reporting group description:	
Subjects received tanezumab 20 mg SC once every 8 weeks for 24 weeks.	

Primary: Change From Baseline in the Daily Average Pain Intensity Numerical Rating Score (NRS) in the Index Bone Metastasis Cancer Pain Site at Week 8

End point title	Change From Baseline in the Daily Average Pain Intensity Numerical Rating Score (NRS) in the Index Bone Metastasis Cancer Pain Site at Week 8
End point description:	
Daily average(avg)pain intensity in index bone metastasis cancer pain site assessed by subjects:11point pain intensity NRS.Range:0(no pain)to10(worst possible pain).Higher scores:more severity of pain.Subjects recorded pain during past 24hours from 0to10 on interactive response technology(IRT)diaries.Baseline daily avg pain intensity value:mean of daily avg pain intensity NRS scores during baseline assessment period(up to 5 days prior dosing)prior to randomisation.Week(wk)8 daily avg pain intensity value:mean of daily avg pain intensity NRS scores recorded for 7 days prior to wk 8.Efficacy data from subjects originally randomised to tanezumab 10mg arm not included in analyses of efficacy as pre-specified in protocol.So,summarised data is not reported for tanezumab 10mg and 10/20mg arms.99999=summarised data not available.Individual values at wk 8 for 10mg: -3,-1.8,-0.6,-3.65,-2.4,-3,-1,-2; for10/20mg: -0.48 respectively.Number of subjects analysed(N)=subjects evaluable	
End point type	Primary
End point timeframe:	
Baseline, Week (wk) 8	

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	8	1	72
Units: Units on a scale				
least squares mean (standard error)	-1.25 (± 0.35)	99999 (± 99999)	99999 (± 99999)	-2.03 (± 0.35)

Statistical analyses

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 8: Analysis of covariance (ANCOVA) model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0381
Method	ANCOVA
Parameter estimate	Differences in least square (LS) mean
Point estimate	-0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.52
upper limit	-0.04
Variability estimate	Standard error of the mean
Dispersion value	0.37

Secondary: Change From Baseline in the Daily Average Pain Intensity NRS score in the Index Bone Metastasis Cancer Pain Site at Weeks 1, 2, 4, 6, 12, 16 and 24

End point title	Change From Baseline in the Daily Average Pain Intensity NRS score in the Index Bone Metastasis Cancer Pain Site at Weeks 1, 2, 4, 6, 12, 16 and 24

End point description:

Daily avg pain intensity in index bone metastasis cancer pain site assessed by subjects:11 point pain intensity NRS.Range:0(no pain)to10(worst possible pain).Higher score:more severity of pain.Subjects noted pain:past 24hours(0to10)onIRT diaries.Baseline daily avg pain intensity value:mean of daily avg pain intensityNRS score during baseline assessment period(upto5days prior to dosing)prior to randomisation.Wk1,2,4,6,12,16,24daily avg pain intensity value:mean of daily avg pain intensityNRS score for7days prior to each wk.99999=summarised data not available.Individual values at specified wk for10mg:0,0.2,-2.42,-0.45,-2.08,-0.4,-,0.14,0, 0,-0.08,-3.4,-0.45,-2.3,-0.4,0,0,0,-0.14,-0.5,-2,-0.74,-4.08,-1.4,0,-0.71,-1.14,-2,-0.94,-0.88,-2.94,-1.97,-3,-1,-2,-3.76,-1.8,-2.5,0.9,-2.22,-2.4,-1.75,-0.5,-2.75,-4,-2.3,-1.3,-1.9,-1,-1.33,-3,-4,-1.8,-2.55,-1.15,-3,-3;10/20mg:-0.62,-1.2,-0.91,-0.62,-2.2,respectively.99999=no subjects. Here,'n'=subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1, 2, 4, 6, 12, 16 and 24

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	9	1	72
Units: Units on a scale				
least squares mean (standard error)				

Change at Week 1 (n=73,9,1,72)	-0.40 (± 0.16)	99999 (± 99999)	99999 (± 99999)	-0.76 (± 0.17)
Change at Week 2 (n=73,9,1,72)	-0.72 (± 0.23)	99999 (± 99999)	99999 (± 99999)	-1.38 (± 0.23)
Change at Week 4 (n=73,9,1,72)	-1.03 (± 0.29)	99999 (± 99999)	99999 (± 99999)	-1.77 (± 0.31)
Change at Week 6 (n=73,8,1,72)	-1.17 (± 0.33)	99999 (± 99999)	99999 (± 99999)	-2.04 (± 0.34)
Change at Week 12 (n=73,9,1,72)	-1.51 (± 0.37)	99999 (± 99999)	99999 (± 99999)	-2.10 (± 0.37)
Change at Week 16 (n=73,7,1,72)	-1.37 (± 0.40)	99999 (± 99999)	99999 (± 99999)	-1.92 (± 0.42)
Change at Week 24 (n=73,6,1,72)	-1.04 (± 0.44)	99999 (± 99999)	99999 (± 99999)	-1.62 (± 0.43)

Statistical analyses

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 1: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0497
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.72
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 2: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0092
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.16
upper limit	-0.17
Variability estimate	Standard error of the mean
Dispersion value	0.25

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 4: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0218
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.37
upper limit	-0.11
Variability estimate	Standard error of the mean
Dispersion value	0.32

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 6: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0154
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.58
upper limit	-0.17
Variability estimate	Standard error of the mean
Dispersion value	0.36

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 12: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1289
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.36
upper limit	0.17
Variability estimate	Standard error of the mean
Dispersion value	0.39

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 16: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.211
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.43
upper limit	0.32
Variability estimate	Standard error of the mean
Dispersion value	0.44

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 24: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2049
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	0.32
Variability estimate	Standard error of the mean
Dispersion value	0.46

Secondary: Change From Baseline in the Daily Worst Pain Intensity NRS Score in the Index Bone Metastasis Cancer Pain Site at Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point title	Change From Baseline in the Daily Worst Pain Intensity NRS Score in the Index Bone Metastasis Cancer Pain Site at Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point description:

Daily worst pain intensity assessed by subjects:11point pain intensity NRS.Range:0(no pain)to10(worst possible pain).Higher scores:more severe pain.Subjects noted pain:past 24hours(0to10)onIRT diaries.Baseline daily worst pain intensity:mean of daily worst pain intensityNRS score during baseline assessment period(upto 5days prior to dosing)before randomisation.Wk1,2,4,6,8,12,16,24 daily worst pain intensity value:mean of daily worst pain intensity NRS scores noted for7days prior to each wk.99999=summarised data not available.Individual values:each wk:10mg:0.4,0.2,-2.85,-0.4,-1.8,-0.4,0,0.45,0,0.4,-0.08,-4,-0.25,-2.37,-0.4,0,0.6,0,-0.02,-0.51,-1.85,-0.4,-4.08,-1.4,0,0.02,-1.14,

-2.74,-0.94,-0.54,-2.94,-1.97,-3,-0.4,-2,-4.6,-1.51,-0.4,-3.65,-2.4,-3,-0.25,-2, -4.63,-1.8,-3.5,0.6,-2.22,-2.4,-1.75,0.1,-2.75,-4.6,-2.3,-1.3,-1.9,-1,-0.73,-3,-4.9,-1.8,-2.55,-1.15,-5.4,-3;10/20 mg:-1.42,-1.57,-1.42,-1.14,-0.85-2.99999=no subjects. Here,'n'=subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	9	1	72
Units: Units on a scale				
least squares mean (standard error)				
Change at Week 1 (n=73,9,1,72)	-0.52 (± 0.18)	99999 (± 99999)	99999 (± 99999)	-0.84 (± 0.19)
Change at Week 2 (n=73,9,1,72)	-0.74 (± 0.25)	99999 (± 99999)	99999 (± 99999)	-1.47 (± 0.25)
Change at Week 4 (n=73,9,1,72)	-1.14 (± 0.30)	99999 (± 99999)	99999 (± 99999)	-1.88 (± 0.31)
Change at Week 6 (n=73,8,1,72)	-1.20 (± 0.33)	99999 (± 99999)	99999 (± 99999)	-2.08 (± 0.34)
Change at Week 8 (n=73,9,1,72)	-1.38 (± 0.36)	99999 (± 99999)	99999 (± 99999)	-2.14 (± 0.37)
Change at Week 12 (n=73,9,1,72)	-1.53 (± 0.36)	99999 (± 99999)	99999 (± 99999)	-2.25 (± 0.38)
Change at Week 16 (n=73,7,1,72)	-1.32 (± 0.44)	99999 (± 99999)	99999 (± 99999)	-2.06 (± 0.43)
Change at Week 24 (n=73,6,1,72)	-1.10 (± 0.44)	99999 (± 99999)	99999 (± 99999)	-1.90 (± 0.45)

Statistical analyses

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 1: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1103
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	0.07

Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 4:ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0236
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.39
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.33

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 2: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0084
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.26
upper limit	-0.19
Variability estimate	Standard error of the mean
Dispersion value	0.27

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 6: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0155
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.59
upper limit	-0.17
Variability estimate	Standard error of the mean
Dispersion value	0.36

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 8: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0505
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.52
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.38

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 12: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0761
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.52
upper limit	0.08
Variability estimate	Standard error of the mean
Dispersion value	0.4

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 16: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1263
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0.21
Variability estimate	Standard error of the mean
Dispersion value	0.48

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 24: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1051
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.76
upper limit	0.17
Variability estimate	Standard error of the mean
Dispersion value	0.49

Secondary: Change From Baseline in the Weekly Average Pain Intensity NRS Score in Non-Index Cancer Pain Sites at Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point title	Change From Baseline in the Weekly Average Pain Intensity NRS Score in Non-Index Cancer Pain Sites at Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point description:

Weekly avg pain intensity in non-index cancer pain site(most painful cancer pain sites other than index bone metastasis cancer pain site) was assessed by subjects on NRS ranging 0=no pain to 10=worst possible pain, higher scores: more severity of pain. Subjects described weekly pain at painful site, scores 0 to 10 on IRT diaries. Baseline weekly avg pain intensity: weekly avg pain intensity NRS score recorded on any day during baseline assessment period (5 days prior to dosing). Wk 1, 2, 4, 6, 8, 12, 16 and 24 weekly avg pain intensity value: weekly avg pain intensity NRS scores recorded on any day from span of 7 days prior to specified wk. mITT set analyzed. Multiple imputation applied. 99999=summarised data not available. Individual values at wk 1,2,4,6,8,12,16 and 24, for 10 mg: 1,0.5,-1,0,-1,-3,-2,-3,-2,-1.375,-2,-1.375,-2; for 10/20 mg: 0,1.5,0.5,0,-2,-1 respectively. 99999=no subjects analysed. N:subjects evaluable for endpoint. n:subjects evaluable at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	2	1	32
Units: Units on a scale				
least squares mean (standard error)				
Change at Week 1 (n=23, 1, 1, 32)	-0.64 (± 0.42)	99999 (± 99999)	99999 (± 99999)	-1.14 (± 0.35)

Change at Week 2 (n=23, 1, 1, 32)	-0.96 (± 0.54)	99999 (± 99999)	99999 (± 99999)	-1.81 (± 0.47)
Change at Week 4 (n=23, 2, 1, 32)	-1.42 (± 0.59)	99999 (± 99999)	99999 (± 99999)	-2.22 (± 0.52)
Change at Week 6 (n=23, 2, 1, 32)	-1.76 (± 0.65)	99999 (± 99999)	99999 (± 99999)	-2.24 (± 0.56)
Change at Week 8 (n=23, 2, 1, 32)	-1.79 (± 0.70)	99999 (± 99999)	99999 (± 99999)	-2.34 (± 0.62)
Change at Week 12 (n=23, 2, 1, 32)	-1.64 (± 0.59)	99999 (± 99999)	99999 (± 99999)	-2.14 (± 0.53)
Change at Week 16 (n=23, 2, 0, 32)	-1.06 (± 0.71)	99999 (± 99999)	99999 (± 99999)	-2.27 (± 0.60)
Change at Week 24 (n=23, 1, 0, 32)	-0.87 (± 0.68)	99999 (± 99999)	99999 (± 99999)	-1.92 (± 0.59)

Statistical analyses

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 1: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3003
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.47
upper limit	0.47
Variability estimate	Standard error of the mean
Dispersion value	0.48

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 2: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1603
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.03
upper limit	0.35
Variability estimate	Standard error of the mean
Dispersion value	0.59

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 4: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2298
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.13
upper limit	0.53
Variability estimate	Standard error of the mean
Dispersion value	0.66

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 6: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5054
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.93
upper limit	0.97
Variability estimate	Standard error of the mean
Dispersion value	0.72

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 8: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4793
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	1.01
Variability estimate	Standard error of the mean
Dispersion value	0.77

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 12: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4496
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.83
upper limit	0.83
Variability estimate	Standard error of the mean
Dispersion value	0.66

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 16: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1263
Method	ANCOVA
Parameter estimate	Difference in least square LS mean
Point estimate	-1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.77
upper limit	0.36
Variability estimate	Standard error of the mean
Dispersion value	0.77

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 24: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.162
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.54
upper limit	0.44
Variability estimate	Standard error of the mean
Dispersion value	0.73

Secondary: Change From Baseline in the Weekly Worst Pain Intensity NRS Score in Non-Index Cancer Pain Sites at Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point title	Change From Baseline in the Weekly Worst Pain Intensity NRS Score in Non-Index Cancer Pain Sites at Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point description:

Weekly worst pain intensity in non-index cancer pain site(most painful cancer pain sites other than index bone metastasis cancer pain site)assessed by subjects on NRS ranging 0=no pain to 10=worst possible pain, higher scores: more severe pain. Subjects described their weekly worst pain at painful site from 0 to 10. Baseline weekly worst pain intensity: weekly worst pain intensity NRS score recorded on any day during baseline assessment period (5 days prior to dosing). Wk 1, 2, 4, 6, 8, 12, 16 and 24 weekly worst pain intensity value was weekly worst pain intensity NRS scores recorded on any day in 7 days prior to specified wk. mITT set analyzed. Multiple imputation applied. 99999: summarised data not available. Individual values at Wk 1,2,4,6,8,12,16 and 24, for 10 mg: 1, 0.5, -1, 0,-1,-3,-2,-3, -2,-1.75, -2 -1.625,-2; for 10/20 mg: -0.5, 0.5,0 0.5,-1 and -0.5 respectively. 99999:no subjects analysed. N:subjects evaluable for endpoint. n:subjects evaluable at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	2	1	32
Units: Units on a scale				
least squares mean (standard error)				
Change at Week 1 (n=23, 1, 1, 32)	-0.43 (± 0.50)	99999 (± 99999)	99999 (± 99999)	-1.50 (± 0.42)
Change at Week 2 (n=23, 1, 1, 32)	-0.34 (± 0.59)	99999 (± 99999)	99999 (± 99999)	-2.30 (± 0.51)
Change at Week 4 (n=23, 2, 1, 32)	-1.18 (± 0.66)	99999 (± 99999)	99999 (± 99999)	-2.62 (± 0.56)
Change at Week 6 (n=23, 2, 1, 32)	-1.62 (± 0.73)	99999 (± 99999)	99999 (± 99999)	-2.50 (± 0.61)
Change at Week 8 (n=23, 2, 1, 32)	-1.77 (± 0.74)	99999 (± 99999)	99999 (± 99999)	-2.54 (± 0.64)

Change at Week 12 (n=23, 2, 1, 32)	-1.36 (± 0.68)	99999 (± 99999)	99999 (± 99999)	-2.56 (± 0.57)
Change at Week 16 (n=23, 2, 0, 32)	-0.85 (± 0.82)	99999 (± 99999)	99999 (± 99999)	-2.75 (± 0.66)
Change at Week 24 (n=23, 1, 0, 32)	-0.73 (± 0.79)	99999 (± 99999)	99999 (± 99999)	-2.35 (± 0.67)

Statistical analyses

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 1: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the non-index cancer pain sites and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0575
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.17
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.54

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 2: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the non-index cancer pain sites and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0031
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-1.96

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.22
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.62

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 4: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the non-index cancer pain sites and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.041
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.82
upper limit	-0.06
Variability estimate	Standard error of the mean
Dispersion value	0.68

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 6: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the non-index cancer pain sites and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2598
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.88

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.44
upper limit	0.68
Variability estimate	Standard error of the mean
Dispersion value	0.77

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 8: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the non-index cancer pain sites and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3426
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.38
upper limit	0.85
Variability estimate	Standard error of the mean
Dispersion value	0.8

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 12: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the non-index cancer pain sites and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1034
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-1.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.65
upper limit	0.26
Variability estimate	Standard error of the mean
Dispersion value	0.72

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 16: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the non-index cancer pain sites and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.029
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-1.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	-0.21
Variability estimate	Standard error of the mean
Dispersion value	0.84

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 24: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the non-index cancer pain sites and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.06
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-1.62

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.31
upper limit	0.07
Variability estimate	Standard error of the mean
Dispersion value	0.83

Secondary: Change From Baseline in the Daily Average Pain Intensity NRS score in the Non-Index Visceral Cancer Pain Sites at Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point title	Change From Baseline in the Daily Average Pain Intensity NRS score in the Non-Index Visceral Cancer Pain Sites at Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point description:

Daily avg pain intensity in the non-index visceral cancer pain site was assessed by participants on an 11 point pain intensity NRS ranging from 0 (no pain) to 10 (worst possible pain), where higher scores signified more severity of pain. The subjects described their pain at the painful site during the past 24 hours by choosing the appropriate number from 0 to 10 on IRT diaries. Baseline is defined as the mean average daily pain intensity NRS score during the baseline assessment period prior to randomisation. The Weeks 1, 2, 4, 6, 8, 12, 16 and 24 pain intensity value is the mean of the daily avg pain intensity scores for the 7 days prior to each specified week. Subject with non-index visceral cancer pain sites were less than 10, hence data was not collected and analysis was not performed for this end point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[1]	0[2]	0[3]	0[4]
Units: Units on a scale				
least squares mean (standard error)	()	()	()	()

Notes:

[1] - Non-index visceral cancer pain sites subject= <10,so,data not collected,analysed for the end point.

[2] - Non-index visceral cancer pain sites subject= <10,so,data not collected,analysed for the end point.

[3] - Non-index visceral cancer pain sites subject= <10,so,data not collected,analysed for the end point.

[4] - Non-index visceral cancer pain sites subject= <10,so,data not collected,analysed for the end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Daily Worst Pain Intensity NRS Score in the Non-Index Visceral Cancer Pain Sites at Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point title	Change From Baseline in the Daily Worst Pain Intensity NRS Score in the Non-Index Visceral Cancer Pain Sites at Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point description:

Daily worst pain intensity in the index bone metastasis cancer pain site was assessed by subjects on an 11 point pain intensity NRS ranging from 0 (no pain) to 10 (worst possible pain), where higher scores signified more severity of pain. The subjects recorded their daily worst pain at the painful site during the

past 24 hours by choosing the appropriate number from 0 to 10 on IRT diaries. Baseline pain intensity value was mean of the daily worst pain intensity NRS scores during the baseline assessment period prior to randomisation. Baseline assessment period was up to 5 days prior to dosing. The Weeks 1, 2, 4, 6, 8, 12, 16 and 24 pain intensity value is the mean of the daily worst pain intensity scores for the 7 days prior to the each specified week. Subject with non-index visceral cancer pain sites were less than 10, hence data was not collected and analysis was not performed for this end point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[5]	0[6]	0[7]	0[8]
Units: Units on a scale				
least squares mean (standard error)	()	()	()	()

Notes:

[5] - Non-index visceral cancer pain sites subject= <10,so,data not collected,analysed for the end point.

[6] - Non-index visceral cancer pain sites subject= <10,so,data not collected,analysed for the end point.

[7] - Non-index visceral cancer pain sites subject= <10,so,data not collected,analysed for the end point.

[8] - Non-index visceral cancer pain sites subject= <10,so,data not collected,analysed for the end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Cumulative Reduction of >=30, 50, 70 and 90 Percent (%) From Baseline in Daily Average Pain Intensity NRS Score in the Index Bone Metastasis Cancer Pain Site at Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point title	Number of Subjects With Cumulative Reduction of >=30, 50, 70 and 90 Percent (%) From Baseline in Daily Average Pain Intensity NRS Score in the Index Bone Metastasis Cancer Pain Site at Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point description:

Daily avg pain intensity in index bone metastasis cancer pain site assessed by subjects:11 point pain intensity NRS. Range:0(no pain) to 10(worst possible pain),higher scores=more severe pain. Subjects recorded daily average pain at painful site during the past 24 hours by choosing the appropriate number from 0 to 10 on IRT diaries. Wk 1, 2, 4, 6, 8, 12, 16 and 24 pain intensity value=mean of the daily avg pain intensity NRS scores for the 7 days prior to each week. Number of subjects with cumulative reduction of >=30,50,70,90 % in daily avg pain intensity NRS score in the index bone metastasis cancer pain site from Baseline to Wk 1, 2, 4, 6, 8, 12, 16 and 24 were reported. Subjects might be reported more than once in the specified rows for a time point. Rows with only non-zero data for cumulative reduction at specified time points, for at least 1 reporting arm, are reported below. Here, 'N': subjects evaluable for this end point and 'n': subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	9	1	71
Units: Subjects				
Week 1: Reduction of >=30% (n=73,9,1,71)	8	2	0	9
Week 1: Reduction of >=50% (n=73,9,1,71)	4	0	0	4
Week 1: Reduction of >=70% (n=73,9,1,71)	0	0	0	1
Week 2: Reduction of >=30% (n=73,9,1,71)	11	2	0	18
Week 2: Reduction of >=50% (n=73,9,1,71)	3	1	0	13
Week 2: Reduction of >=70%(n=73,9,1,71)	0	0	0	4
Week 2: Reduction of >=90%(n=73,9,1,71)	0	0	0	2
Week 4: Reduction of >=30%(n=73,9,1,71)	18	2	0	25
Week 4: Reduction of >=50%(n=73,9,1,71)	6	1	0	16
Week 4: Reduction of >=70%(n=73,9,1,71)	2	1	0	9
Week 4: Reduction of >=90%(n=73,9,1,71)	0	0	0	3
Week 6: Reduction of >=30%(n=73,9,1,71)	20	5	0	30
Week 6: Reduction of >=50%(n=73,9,1,71)	6	1	0	19
Week 6: Reduction of >=70% (n=73,8,1,71)	2	0	0	10
Week 6: Reduction of >=90%(n=73,9,1,71)	0	0	0	3
Week 8: Reduction of >=30% (n=73,8,1,71)	19	5	0	28
Week 8: Reduction of >=50%(n=73,9,1,71)	9	2	0	18
Week 8: Reduction of >=70%(n=73,9,1,71)	3	0	0	9
Week 8: Reduction of >=90%(n=73,9,1,71)	1	0	0	5
Week 12: Reduction of >=30%(n=73,9,1,71)	21	5	1	32
Week 12: Reduction of >=50%(n=73,9,1,71)	12	2	0	21
Week 12: Reduction of >=70%(n=73,9,1,71)	6	1	0	10
Week 12: Reduction of >=90%(n=73,9,1,71)	2	0	0	5
Week 16: Reduction of >=30% (n=73,7,1,71)	17	2	0	27
Week 16: Reduction of >=50%(n=73,9,1,71)	12	2	0	19
Week 16: Reduction of >=70%(n=73,9,1,71)	7	1	0	12
Week 16: Reduction of >=90%(n=73,9,1,71)	5	0	0	5
Week 24: Reduction of >=30% (n=73,6,1,71)	16	4	0	27

Week 24: Reduction of >=50%(n=73,9,1,71)	10	3	0	19
Week 24: Reduction of >=70%(n=73,9,1,71)	5	2	0	11
Week 24: Reduction of >=90%(n=73,9,1,71)	3	1	0	4

Statistical analyses

Statistical analysis title	Placebo vs Tanezumab 20mg
Statistical analysis description:	
Week 1 Reduction >=30%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).	
Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8054
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	3.18

Statistical analysis title	Placebo vs Tanezumab 20mg
Statistical analysis description:	
Week 1 Reduction >=70%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).	
Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9565
Method	Regression, Logistic

Statistical analysis title	Placebo vs Tanezumab 20mg
Statistical analysis description:	
Week 1 Reduction >=50%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).	
Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9292
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	3.98

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 2 Reduction >=30%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1429
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	4.36

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 2 Reduction >=90%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9489
Method	Regression, Logistic

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 2 Reduction >=70%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.945
Method	Regression, Logistic

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 2 Reduction >=50%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.014
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	19.31

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 4 Reduction >=30%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1932
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	3.39

Statistical analysis title	Placebo vs Tanezumab 20mg
Statistical analysis description:	
Week 4 Reduction >=50%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).	
Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0254
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.15
upper limit	8.74

Statistical analysis title	Placebo vs Tanezumab 20mg
Statistical analysis description:	
Week 4 Reduction >=70%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).	
Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0455
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	24.16

Statistical analysis title	Placebo vs Tanezumab 20mg
Statistical analysis description:	
Week 4 Reduction >=90%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).	
Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9464
Method	Regression, Logistic

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 6 Reduction >=30%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0969
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	3.72

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 6 Reduction >=50%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0043
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.58
upper limit	11.74

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 6 Reduction >=70%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0352
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.13
upper limit	26.75

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 6 Reduction >=90%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9464
Method	Regression, Logistic

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 8 Reduction >=30%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1471
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	3.52

Statistical analysis title	Placebo vs Tanezumab 20mg
Statistical analysis description: Week 8 Reduction >=70%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).	
Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0993
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	12.83

Statistical analysis title	Placebo vs Tanezumab 20mg
Statistical analysis description: Week 8 Reduction >=50%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).	
Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0405
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	6.22

Statistical analysis title	Placebo vs Tanezumab 20mg
Statistical analysis description: Week 8 Reduction >=90%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).	
Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1726
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	43.64

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 12 Reduction >=30%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0918
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	3.74

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 12 Reduction >=50%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0704
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.13

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	4.82

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 12 Reduction >=70%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3569
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	5.01

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 12 Reduction >=90%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3062
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	13.79

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 16 Reduction >=30%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1058
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	3.85

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 16 Reduction >=50%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1571
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	4.14

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 16 Reduction >=90%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8867
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.24
upper limit	3.46

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 16 Reduction >=70%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2454
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	5.24

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 24 Reduction >=30%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0689
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	4.21

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 24 Reduction >=50%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0568
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	5.44

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 24 Reduction >=70%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1268
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	7.46

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 24 Reduction >=90%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7971
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	6

Secondary: Number of Subjects With Reduction of >=30, 50, 70 and 90% From Baseline in Daily Worst Pain Intensity NRS Score in the Index Bone Metastasis Cancer Pain Site at Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point title	Number of Subjects With Reduction of >=30, 50, 70 and 90% From Baseline in Daily Worst Pain Intensity NRS Score in the Index Bone Metastasis Cancer Pain Site at Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point description:

Daily worst pain intensity in index bone metastasis cancer pain site assessed by subjects:11 point pain intensity NRS. Range:0(no pain) to10(worst possible pain), higher scores = more severe pain. Subjects recorded daily worst pain at painful site during past 24 hours by choosing appropriate number from 0 to 10 on IRT diaries. Wk 1, 2, 4, 6, 8, 12, 16 and 24 pain intensity value = mean of the daily worst pain intensity NRS scores for the 7 days prior to each wk. Number of subjects with cumulative reduction of >= 30,50,70,90 % in daily worst pain intensity NRS score in the index bone metastasis cancer pain site from Baseline to Wk 1, 2, 4, 6, 8, 12, 16 and 24 were reported. Subjects might be reported more than once in the specified rows for a time point. Rows with only non-zero data for cumulative reduction at specified time points, for at least 1 reporting arm, are reported below. Here, 'N': subjects evaluable for this end point and 'n': subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	9	0[9]	71
Units: Subjects				
Week 1: Reduction of >=30%	7	2		9
Week 1: Reduction of >=50%	1	0		3
Week 1: Reduction of >=70%	0	0		2
Week 1: Reduction of >=90%	0	0		0
Week 2: Reduction of >=30%	9	2		17
Week 2: Reduction of >=50%	2	1		8

Week 2: Reduction of >=70%	0	0		5
Week 2: Reduction of >=90%	0	0		2
Week 4: Reduction of >=30%	12	1		21
Week 4: Reduction of >=50%	5	1		14
Week 4: Reduction of >=70%	0	1		6
Week 4: Reduction of >=90%	0	0		2
Week 6: Reduction of >=30%	13	4		26
Week 6: Reduction of >=50%	4	1		14
Week 6: Reduction of >=70%	2	0		7
Week 6: Reduction of >=90%	0	0		2
Week 8: Reduction of >=30%	14	5		24
Week 8: Reduction of >=50%	7	2		16
Week 8: Reduction of >=70%	2	0		8
Week 8: Reduction of >=90%	2	0		2
Week 12: Reduction of >=30%	16	5		24
Week 12: Reduction of >=50%	8	2		16
Week 12: Reduction of >=70%	5	1		7
Week 12: Reduction of >=90%	2	0		4
Week 16: Reduction of >=30%	11	2		24
Week 16: Reduction of >=50%	9	2		18
Week 16: Reduction of >=70%	7	0		11
Week 16: Reduction of >=90%	3	0		3
Week 24: Reduction of >=30%	11	4		25
Week 24: Reduction of >=50%	9	3		18
Week 24: Reduction of >=70%	4	2		9
Week 24: Reduction of >=90%	2	0		3

Notes:

[9] - No subjects met criteria for data collection and analysis for 10/20 mg for this end point.

Statistical analyses

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 1 Reduction >=30%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6658
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	3.7

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 1 Reduction >=50%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3443
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	31.35

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 1 Reduction >=70%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9527
Method	Regression, Logistic

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 2 Reduction >=30%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0757
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	5.5

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 2 Reduction >=50%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0659
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	22.42

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 2 Reduction >=70%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.938
Method	Regression, Logistic

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 2 Reduction >=90%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9493
Method	Regression, Logistic

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 4 Reduction >=30%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0914
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	4.59

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 4 Reduction >=50%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0359
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.22

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	9.61

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 4 Reduction >=70%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9538
Method	Regression, Logistic

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 4 Reduction >=90%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9493
Method	Regression, Logistic

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 6 Reduction >=30%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0143
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.66

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.22
upper limit	5.8

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 6 Reduction >=50%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0176
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.28
upper limit	13.74

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 6 Reduction >=70%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1298
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	18.06

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 6 Reduction >=90%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9493
Method	Regression, Logistic

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 8 Reduction >=30%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0527
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	4.67

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 8 Reduction >=70%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0994
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.91

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	19.76

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 8 Reduction >=50%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0457
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	7.12

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 8 Reduction >=90%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6977
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.07
upper limit	5.86

Statistical analysis title	Placebo vs Tanezumab 20mg
Statistical analysis description:	
Week 12 Reduction >=30%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).	
Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.146
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	3.75

Statistical analysis title	Placebo vs Tanezumab 20mg
Statistical analysis description:	
Week 12 Reduction >=50%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).	
Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0742
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	6.01

Statistical analysis title	Placebo vs Tanezumab 20mg
Statistical analysis description:	
Week 12 Reduction >=70%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).	
Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5565
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	4.91

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 12 Reduction >=90%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5623
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	10.35

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 16 Reduction >=30%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0116
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.86

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.27
upper limit	6.47

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 16 Reduction >=50%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0615
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	5.7

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 16 Reduction >=90%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9946
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	5.33

Statistical analysis title	Placebo vs Tanezumab 20mg
Statistical analysis description:	
Week 16 Reduction >=70%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).	
Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3316
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	4.8

Statistical analysis title	Placebo vs Tanezumab 20mg
Statistical analysis description:	
Week 24 Reduction >=30%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).	
Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0083
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.33
upper limit	6.76

Statistical analysis title	Placebo vs Tanezumab 20mg
Statistical analysis description:	
Week 24 Reduction >=50%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).	
Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0513
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	5.88

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 24 Reduction >=70%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1528
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	8.58

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 24 Reduction >=90%: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7251
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.41

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	9.65

Secondary: Change From Baseline in Subjects Global Assessment of Cancer Pain (PGA-CP) at Weeks 2, 4, 8, 16 and 24

End point title	Change From Baseline in Subjects Global Assessment of Cancer Pain (PGA-CP) at Weeks 2, 4, 8, 16 and 24

End point description:

Subjects at specified time points were asked: "Considering all ways your cancer pain affects you,how are you doing today?" on a Likert scale range: 1 to 5, on IRT diaries. Scores:1=very good(asymptomatic and no limitation of normal activities); 2=good(mild symptoms and no limitation of normal activities); 3= fair(moderate symptoms and limitation of some normal activities); 4= poor(severe symptoms,inability to carry out most normal activities); 5=very poor(very severe symptoms which are intolerable and inability to carry out all normal activities). Higher scores: worsening of condition. mITT set analysed. Multiple imputation applied. 99999=summarised data not available. Individual values at wk 2,4,8,16,24 for 10mg: 0, 0, -3, 0, -2, 1, 0, -1,-1, 0, 1, 0, 0, -3, 1, 0, 0, -1, -1, 0, -1, 0, -3, 1, 0, -1, -1, -2, 0, -3, 1, 0,-1, -1, 0, -3, 1, 2,-1; for 10/20 mg: 1,0,1 respectively. 99999=no subjects analysed. N:subjects evaluable for endpoint. n:subjects evaluable at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 16 and 24

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	9	1	71
Units: Units on a scale				
least squares mean (standard error)				
Change at Week 2 (n=73, 1, 71,9)	-0.39 (± 0.11)	99999 (± 99999)	99999 (± 99999)	-0.43 (± 0.12)
Change at Week 4 (n=73, 1, 71,9)	-0.36 (± 0.14)	99999 (± 99999)	99999 (± 99999)	-0.66 (± 0.14)
Change at Week 8 (n=73, 1, 71,9)	-0.23 (± 0.16)	99999 (± 99999)	99999 (± 99999)	-0.56 (± 0.17)
Change at Week 16 (n=73,0,71,6)	-0.16 (± 0.16)	99999 (± 99999)	99999 (± 99999)	-0.32 (± 0.17)
Change at Week 24 (n=73,0,71,6)	-0.19 (± 0.18)	99999 (± 99999)	99999 (± 99999)	-0.29 (± 0.17)

Statistical analyses

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 2: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline global assessment score, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7045
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	0.19
Variability estimate	Standard error of the mean
Dispersion value	0.12

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 4: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline global assessment score, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0402
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.59
upper limit	-0.01
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 8: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline global assessment score, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0637
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.67
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 16: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline global assessment score, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3804
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Change at Week 24: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline global assessment score, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates.

Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5894
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	0.27
Variability estimate	Standard error of the mean
Dispersion value	0.18

Secondary: Number of Subjects With Reduction of >=2 Points From Baseline in PGA-CP Scores at Weeks 2, 4, 8, 16 and 24

End point title	Number of Subjects With Reduction of >=2 Points From Baseline in PGA-CP Scores at Weeks 2, 4, 8, 16 and 24

End point description:

Subjects at specified time points, answered to the following question, "Considering all the way your cancer pain affects you, how are you doing today?" on a Likert scale ranging from 1 to 5, on IRT diaries. Scores:1= very good (asymptomatic and no limitation of normal activities); 2= good(mild symptoms and no limitation of normal activities); 3= fair(moderate symptoms and limitation of some normal activities); 4= poor (severe symptoms and inability to carry out most normal activities); and 5= very poor (very severe symptoms which are intolerable and inability to carry out all normal activities). Higher scores: worsening of condition. Efficacy data from subjects who were originally randomised to tanezumab 10 mg arm were not included in analyses of efficacy as pre-specified in protocol. So, summarised data is not reported for tanezumab 10 mg and 10/20 mg arms. Reported individual values. Here, 'n': subjects evaluable at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 16 and 24

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	9	1	72
Units: Subjects				
Week 2 (n=73,9,1,72)	7	2	0	5
Week 4 (n=73,9,1,72)	9	1	0	11
Week 8 (n=73,9,1,72)	10	1	0	12
Week 16 (n=73,6,1,72)	9	2	0	12
Week 24 (n=73,6,1,72)	9	1	0	11

Statistical analyses

Statistical analysis title	Placebo vs Tanezumab 20mg
Statistical analysis description:	
Week 2: Logistic regression model included baseline PGA-CP, baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).	
Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2033
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	1.69

Statistical analysis title	Placebo vs Tanezumab 20mg
Statistical analysis description:	
Week 4: Logistic regression model included baseline PGA-CP, baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).	
Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7627
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	3.41

Statistical analysis title	Placebo vs Tanezumab 20mg
Statistical analysis description:	
Week 8: Logistic regression model included baseline PGA-CP, baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).	
Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6894
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	3.43

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 16: Logistic regression model included baseline PGA-CP, baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5905
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	3.83

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 24: Logistic regression model included baseline PGA-CP, baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8354
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.12

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	3.35

Secondary: Average Daily Total Opioid Consumption at Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point title	Average Daily Total Opioid Consumption at Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point description:

In this end point average daily opioid consumption was reported in milligram of morphine equivalent dose (mg of MED). mITT analysis set analysed. LOCF data applied. 99999:summarised data not available. Individual values at wk 1,2,4,6,8,12,16,24 for 10mg: 0.3, 30, 181.54, 1082.74, 122.03, 10, 120, 22.5,30, 0.3, 30, 182.4, 1082.22, 120.96, 10, 120, 22.5,30, 0.3, 34.28, 182.4, 1082.22, 120.96, 52.85, 120, 22.5,30, 0.3, 95, 182.4, 1081.54, 120.96, 10, 137.14, 22.5,30, 0.3, 122.14, 2.4, 1081.71, 120.96, 10, 120, 22.5,30, 0.3, 258.57, 2.4, 1.2, 88.45, 10, 120, 22.5,30, 0.3, 170, 2.4, 1.2, 86.31, 10, 120, 22.5,30, 0.3, 170, 2.4, 1.2, 88.45, 74.28, 120, 18.21,30; for 10/20mg: 510, 510,480, 510, 510, 480, 480, 480 respectively. N:subjects evaluable for endpoint. n:subjects evaluable at specified time points.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	9	1	72
Units: mg of MED				
arithmetic mean (standard deviation)				
Week 1 (n=72,9,1,69)	183.94 (± 275.05)	99999 (± 99999)	99999 (± 99999)	186.86 (± 351.83)
Week 2 (n=73,9,1,69)	177.98 (± 270.67)	99999 (± 99999)	99999 (± 99999)	188.41 (± 356.15)
Week 4 (n=73,9,1,69)	177.87 (± 266.93)	99999 (± 99999)	99999 (± 99999)	181.32 (± 349.82)
Week 6 (n=73,9,1,70)	186.20 (± 280.44)	99999 (± 99999)	99999 (± 99999)	173.45 (± 346.27)
Week 8 (n=73,9,1,70)	188.10 (± 281.01)	99999 (± 99999)	99999 (± 99999)	170.31 (± 327.19)
Week 12 (n=73,9,1,70)	187.43 (± 336.74)	99999 (± 99999)	99999 (± 99999)	177.06 (± 332.39)
Week 16 (n=73,9,1,70)	189.62 (± 333.77)	99999 (± 99999)	99999 (± 99999)	173.48 (± 329.17)
Week 24 (n=73,9,1,70)	189.78 (± 353.10)	99999 (± 99999)	99999 (± 99999)	346.95 (± 1537.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Average Number of Doses of Rescue Opioid Consumption at Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point title	Average Number of Doses of Rescue Opioid Consumption at Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point description:

In this end point average number of doses of rescue opioid consumption at specified time points were reported. mITT analysis set analysed. LOCF data applied. 99999: summarised data not available. Individual values at wk 1,2,4,6,8,12,16,24 for 10mg: 1, 1, 1, 1, 0.14, 1,1, 1, 1, 1, 1, 1, 0.14, 1,1,1, 1, 1, 1, 1, 0.14, 0.14, 0.85,1,1, 1, 1, 1, 0.85, 0.14, 0.14, 1, 1,1, 1, 1, 1, 1, 0.28, 0.14, 0.71, 1,1, 1, 1, 1, 1, 1, 0.14, 0.14, 1,1, 1, 1, 1, 1, 0.85, 0.14, 0.14, 1,1, 1, 1, 1, 1, 1, 0.14, 0.14, 0.42,1; for 10/20mg: 1,1, 0.43, 1, 1, 1, 1, 1 respectively. N:subjects evaluable for endpoint. n:subjects evaluable at specified time points.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 4, 6, 8, 12, 16 and 24

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	9	1	72
Units: Doses				
arithmetic mean (standard deviation)				
Week 1 (n=52,8,1,42)	1.15 (± 0.76)	99999 (± 99999)	99999 (± 99999)	0.96 (± 0.48)
Week 2 (n=54,8,1,44)	1.11 (± 0.69)	99999 (± 99999)	99999 (± 99999)	0.89 (± 0.52)
Week 4 (n=56,9,1,46)	1.08 (± 0.69)	99999 (± 99999)	99999 (± 99999)	0.80 (± 0.57)
Week 6 (n=61,9,1,48)	0.95 (± 0.70)	99999 (± 99999)	99999 (± 99999)	0.80 (± 0.65)
Week 8 (n=61,9,1,48)	0.99 (± 0.72)	99999 (± 99999)	99999 (± 99999)	0.81 (± 0.61)
Week 12 (n=61,9,1,48)	0.92 (± 0.94)	99999 (± 99999)	99999 (± 99999)	0.73 (± 0.57)
Week 16 (n=62,9,1,48)	0.86 (± 0.93)	99999 (± 99999)	99999 (± 99999)	0.75 (± 0.57)
Week 24 (n=65,9,1,49)	0.79 (± 0.93)	99999 (± 99999)	99999 (± 99999)	0.69 (± 0.57)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Weekly Opioid-Related Symptom Distress Scale (OR-SDS) at Weeks 2, 4, 8, 16, and 24

End point title	Change From Baseline in the Weekly Opioid-Related Symptom Distress Scale (OR-SDS) at Weeks 2, 4, 8, 16, and 24

End point description:

OR 12 symptoms(Ss) evaluated. Range:severity(none=0 to very severe=4),distress(none =0 to very much=5);frequency(none =0 to almost constantly =4;subjects reported number of retching/vomiting

episodes(none =0, 1-2 episodes =1, 3-4 episodes =2, 5-6 episodes =3, >6 episodes =4).Frequency(F)composite score:mean of F scores from all Ss, 0(none) to 4(almost constantly);Severity(S) composite score:mean of S scores from all 12 Ss, 0(none) to 4(max severity);Distress(D)composite score:mean of D scores from all 12 symptoms,0(none) to 5(max distress).Multi domain avg(MDA):avg of each Ss for F,S,D; 0(none)to 4.34(worse);higher scores=worse condition in all domains.99999=Individual values at wk 2,4,8,16,24 for 10 mg:-1,0,-1,-0.67,-0.6,0.2,-0.25,-0.22,-0.8,0,-0.25,-0.35,-1,0,-0.75,-0.58;10/20 mg: -1.33,-0.83,0.17,-0.67,-1.5,-0.5,0,-0.67,-1,-0.75,0.25,-0.5 respectively.9999=not analysed. N:subjects evaluable for endpoint. n:subjects at

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 16, and 24

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	2	1	72
Units: Units on a scale				
least squares mean (standard error)				
Change at Week2: F Composite Score (n=73,1,72,1)	-0.06 (± 0.16)	99999 (± 99999)	99999 (± 99999)	-0.11 (± 0.17)
Change at Week 2: S Composite Score (n=73,1,72,1)	-0.18 (± 0.11)	99999 (± 99999)	99999 (± 99999)	-0.02 (± 0.12)
Change at Week 2: D Composite Score (n=73,1,72,1)	-0.08 (± 0.18)	99999 (± 99999)	99999 (± 99999)	0.09 (± 0.19)
Change at Week2:MDA Composite Score (n=73,1,72,1)	-0.10 (± 0.14)	99999 (± 99999)	99999 (± 99999)	-0.02 (± 0.15)
Change at Week 4: F Composite Score (n=73,1,72,1)	-0.19 (± 0.14)	99999 (± 99999)	99999 (± 99999)	-0.12 (± 0.14)
Change at Week 4: S Composite Score (n=73,1,72,1)	-0.10 (± 0.12)	99999 (± 99999)	99999 (± 99999)	-0.01 (± 0.13)
Change at Week 4: D Composite Score (n=73,1,72,1)	0.12 (± 0.15)	99999 (± 99999)	99999 (± 99999)	0.11 (± 0.15)
Change at Week4:MDA Composite Score (n=73,1,72,1)	-0.06 (± 0.12)	99999 (± 99999)	99999 (± 99999)	-0.00 (± 0.13)
Change at Week 8: F Composite Score (n=73,1,72,2)	0.07 (± 0.15)	99999 (± 99999)	99999 (± 99999)	-0.10 (± 0.16)
Change at Week 8: S Composite Score (n=73,1,72,2)	-0.07 (± 0.12)	99999 (± 99999)	99999 (± 99999)	-0.17 (± 0.13)
Change at Week 8: D Composite Score (n=73,1,72,2)	0.03 (± 0.19)	99999 (± 99999)	99999 (± 99999)	0.26 (± 0.20)
Change at Week8:MDA Composite Score (n=73,1,72,2)	0.02 (± 0.13)	99999 (± 99999)	99999 (± 99999)	-0.02 (± 0.14)
Change at Week 16: F Composite Score (n=73,0,72,1)	0.08 (± 0.19)	99999 (± 99999)	99999 (± 99999)	-0.07 (± 0.22)
Change at Week 16: S Composite Score (n=73,0,72,1)	-0.12 (± 0.15)	99999 (± 99999)	99999 (± 99999)	0.08 (± 0.17)
Change at Week 16: D Composite Score (n=73,0,72,1)	0.10 (± 0.20)	99999 (± 99999)	99999 (± 99999)	-0.07 (± 0.24)
Change at Week16:MDA Composite Score(n=73,0,72,1)	0.02 (± 0.16)	99999 (± 99999)	99999 (± 99999)	-0.04 (± 0.19)
Change at Week 24: F Composite Score (n=73,0,72,0)	0.29 (± 0.21)	99999 (± 99999)	99999 (± 99999)	-0.13 (± 0.24)
Change at Week 24: S Composite Score (n=73,0,72,0)	-0.01 (± 0.17)	99999 (± 99999)	99999 (± 99999)	0.16 (± 0.18)
Change at Week24: D Composite Score (n=73,0,72,0)	0.33 (± 0.21)	99999 (± 99999)	99999 (± 99999)	0.22 (± 0.23)
Change at Week24:MDA Composite Score (n=73,0,72,0)	0.17 (± 0.18)	99999 (± 99999)	99999 (± 99999)	0.07 (± 0.20)

Statistical analyses

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 2 Frequency Composite Score: Mixed model for repeated measurements (MMRM) model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS frequency scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8069
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	0.38
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 8 Frequency Composite Score: MMRM model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS frequency scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3933
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	0.23

Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 4 Frequency Composite Score: MMRM model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS frequency scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7127
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	0.41
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 24 Frequency Composite Score: MMRM model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS frequency scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1814
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.05
upper limit	0.21
Variability estimate	Standard error of the mean
Dispersion value	0.3

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 16 Frequency Composite Score: MMRM model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS frequency scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5869
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.71
upper limit	0.41
Variability estimate	Standard error of the mean
Dispersion value	0.28

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 2 Severity Composite Score: MMRM model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS severity scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2822
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0.46
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 4 Severity Composite Score: MMRM model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS severity scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5795
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	0.41
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 16 Severity Composite Score: MMRM model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS severity scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3692
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	0.63
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 8 Severity Composite Score: MMRM model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as

fixed effects, and treatment*time interaction, baseline OR-SDS severity scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5486
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	0.22
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 24 Severity Composite Score: MMRM model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS severity scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4724
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.63
Variability estimate	Standard error of the mean
Dispersion value	0.23

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 2 Distress Composite Score: MMRM model includes time (study week), treatment, region, and randomization stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS distress scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.477
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.64
Variability estimate	Standard error of the mean
Dispersion value	0.23

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 16 Distress Composite Score: MMRM model includes time (study week), treatment, region, and randomization stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS distress scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5607
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.77
upper limit	0.42
Variability estimate	Standard error of the mean
Dispersion value	0.29

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 4 Distress Composite Score: MMRM model includes time (study week), treatment, region, and randomization stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS distress scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9791
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.38
upper limit	0.37
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 8 Distress Composite Score: MMRM model includes time (study week), treatment, region, and randomization stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS distress scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3574
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	0.74
Variability estimate	Standard error of the mean
Dispersion value	0.25

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 24 Distress Composite Score: MMRM model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS distress scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7143
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.68
upper limit	0.47
Variability estimate	Standard error of the mean
Dispersion value	0.28

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 2 MDA Composite Score: MMRM model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS MDA scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6381
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	0.45
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 4 MDA Composite Score: MMRM model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS MDA scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7181
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0.37
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 8 MDA Composite Score: MMRM model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS MDA scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8378
Method	Mixed models analysis
Parameter estimate	Difference in least square (LS) mean
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.38
upper limit	0.31
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 24 MDA Composite Score: MMRM model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS MDA scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg

Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6719
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.25

Statistical analysis title	Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 16 MDA Composite Score: MMRM model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS MDA scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates.

Comparison groups	Placebo v Tanezumab 20 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.795
Method	Mixed models analysis
Parameter estimate	Difference in LS mean
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.52
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.23

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs)

End point description:

An adverse event (AE) was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. Serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent were events between first dose of study drug and up to 24 weeks post last dose that were absent before treatment or that worsened relative to pretreatment state. AEs included both serious and all non-serious AEs. Subjects were followed up to 24 weeks after study drug last dose. The safety analysis set was defined as all subjects treated with tanezumab or placebo SC, including subjects who received tanezumab 10 mg prior to protocol

amendment 3.

End point type	Secondary

End point timeframe:

Day 1 of dosing up to 24 weeks post last dose (maximum up to Week 48)

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	9	1	72
Units: Subjects	52	9	1	62

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Laboratory Abnormalities (Normal Baseline)

End point title	Number of Subjects With Laboratory Abnormalities (Normal Baseline)

End point description:

Lab abnormality criteria:hemoglobin(HGB);hematocrit;erythrocytes< 0.8*lower limit of normal(LLN);erythrocyte mean corpuscular volume/HGB/ HGB conce.,erythrocytes distribution width<0.9*LLN, >1.1*upper(U)LN; platelets<0.5*LLN,>1.75* ULN;leukocytes<0.6*LLN,>1.5*ULN; lymphocytes, neutrophils <0.8*LLN, >1.2*ULN; basophils, eosinophils, monocytes >1.2*ULN; total bilirubin>1.5*ULN; activated partial thromboplastin time, prothrombin time, prothrombin intl. normalized ratio>1.1*ULN; bilirubin >1.5*ULN; aspartate aminotransferase(AT), alanine AT,gamma glutamyl transferase,lactate dehydrogenase,alkaline phosphatase >3.0*ULN; protein;albumin<0.8*LLN, >1.2*ULN; urea nitrogen,creatinine,cholesterol,triglycerides >1.3*ULN; urate >1.2*ULN; sodium <0.95*LLN,>1.05*ULN; potassium,chloride,calcium,magnesium,bicarbonate <0.9*LLN, >1.1*ULN; phosphate <0.8*LLN, >1.2*ULN; Urine:glucose, ketones, protein, HGB, bilirubin, nitrite >=1.Safety analysis set analysed. N:subjects evaluable for endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1, before dosing) up to Week 48

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	8	0[10]	50
Units: Subjects	18	1		20

Notes:

[10] - No subjects met criteria for data collection and analysis for 10/20 mg for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Laboratory Abnormalities (Abnormal Baseline)

End point title	Number of Subjects With Laboratory Abnormalities (Abnormal Baseline)

End point description:

Laboratory abnormality criteria included: HGB; hematocrit; erythrocytes < 0.8* LLN; erythrocyte mean corpuscular volume/HGB/ HGB concentration, erythrocytes distribution width <0.9*LLN, >1.1*upper limit of normal (ULN); platelets <0.5*LLN,>1.75* ULN; leukocytes <0.6*LLN, >1.5*ULN; lymphocytes, neutrophils <0.8*LLN, >1.2*ULN; basophils, eosinophils, monocytes >1.2*ULN; activated partial thromboplastin time, prothrombin time >1.1*ULN; bilirubin>1.5*ULN; aspartate AT, alanine AT, gamma glutamyl transferase, lactate dehydrogenase, alkaline phosphatase >3.0*ULN; protein; albumin<0.8*LLN, >1.2*ULN; urea nitrogen, cholesterol, triglycerides >1.3*ULN; urate >1.2*ULN; sodium <0.95*LLN,>1.05*ULN; potassium, chloride, calcium, magnesium, bicarbonate <0.9*LLN, >1.1*ULN; phosphate <0.8*LLN, >1.2*ULN; glucose <0.6*LLN, >1.5*ULN; creatine kinase >2.0*ULN. Safety analysis set analysed. N:subjects evaluable for endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1, before dosing) up to Week 48

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	8	0[11]	46
Units: Subjects	15	2		14

Notes:

[11] - No subjects met criteria for data collection and analysis for 10/20 mg for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Categorical Change From Baseline to Last Post-Baseline in Sitting Systolic and Diastolic Blood Pressure During Treatment Period

End point title	Number of Subjects With Categorical Change From Baseline to Last Post-Baseline in Sitting Systolic and Diastolic Blood Pressure During Treatment Period

End point description:

Change categories for sitting systolic blood pressure (SBP) measured in millimeter of mercury (mm Hg) were as follows: change <=-40, change >-40 to -30, change >-30 to -20, change >-20 to -10, change >-10 to 0, change >0 to <10, change >=10 to <20, change >=20 to <30, change >=30 to <40 and change >=40. Change categories for sitting diastolic blood pressure (DBP) measured in mm Hg were as follow: change <=-30, change >-30 to -20, change >-20 to -10, change >-10 to 0, change >0 to <10, change >=10 to <20, change >=20 to <30 and change >=30. Rows with only non-zero data/values, for at least 1 reporting arm, are reported below. Safety analysis set: all subjects treated with tanezumab or placebo SC, including subjects received tanezumab 10 mg prior to protocol amendment 3. N:subjects evaluable for endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1, before dosing) up to Week 24

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	9	1	68
Units: Subjects				
Sitting SBP(mmHg)Change <=-40	1	0	0	1
Sitting SBP(mmHg)Change >-40 to -30	1	0	0	2
Sitting SBP(mmHg) Change >-30 to -20	6	0	1	3
Sitting SBP(mmHg) Change >-20 to -10	10	3	0	14
Sitting SBP(mmHg) Change >-10 to 0	26	2	0	25
Sitting SBP(mmHg) Change >0 to <10	12	1	0	9
Sitting SBP(mmHg) Change >=10 to <20	6	3	0	10
Sitting SBP(mmHg) Change >=20 to <30	5	0	0	3
Sitting SBP(mmHg) Change >=30 to <40	0	0	0	1
Sitting DBP (mmHg) Change >-30 to -20	0	1	0	1
Sitting DBP(mmHg) Change >-20 to -10	10	1	1	13
Sitting DBP(mmHg) Change >-10 to 0	39	4	0	26
Sitting DBP(mmHg) Change >0 to <10	11	0	0	18
Sitting DBP(mmHg) Change >=10 to <20	5	2	0	9
Sitting DBP(mmHg) Change >=20 to <30	2	1	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Categorical Summary of Electrocardiogram (ECG) (QTC) Data

End point title	Number of Subjects With Categorical Summary of Electrocardiogram (ECG) (QTC) Data

End point description:

Electrocardiogram assessment included QT interval corrected using Fridericia's formula (QTcF), QT interval corrected using Bazett's formula (QTcB), both had following categories: 450<=Value<480 millisecond (msec), 480<=Value<500 msec and Value>=500 msec. Safety analysis set: all subjects treated with tanezumab or placebo SC, including subjects received tanezumab 10 mg prior to protocol amendment 3. In reporting arm “Tanezumab10/20 mg”, the subject did not have post-baseline results evaluated against ECG (QTC) criteria, hence was not evaluable for this end point. N:subjects evaluable for endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1, before dosing) up to Week 24

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	8	0[12]	44
Units: Subjects				
QTCB Interval 450<=Value<480	2	1		6
QTCB Interval 480<=Value<500	0	0		1
QTCF Interval 450<=Value<480	1	0		5

Notes:

[12] - No subjects met criteria for data collection and analysis for 10/20 mg for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Confirmed Orthostatic Hypotension

End point title	Number of Subjects with Confirmed Orthostatic Hypotension

End point description:

Orthostatic hypotension was defined as postural change (supine to standing) that met the following criteria: for systolic blood pressure (BP) less than or equal to (<=) 150 millimeter of mercury (mmHg) (mean supine): reduction in systolic BP >=20 mmHg or reduction in diastolic BP >=10 mmHg at the 1 and/or 3 minute standing BP measurements. For systolic BP greater than (>) 150 mmHg (mean supine): reduction in systolic BP >=30 mmHg or reduction in diastolic BP >=15 mmHg at the 1 and/or 3 minute standing BP measurements. If the 1 minute or 3 minute standing BP in a sequence met the orthostatic hypotension criteria, then that sequence was considered positive. If 2 of 2 or 2 of 3 sequences were positive, then orthostatic hypotension was considered confirmed. Safety analysis set: all subjects treated with tanezumab or placebo SC, including subjects received tanezumab 10 mg prior to protocol amendment 3. N:subjects evaluable for endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1, before dosing), Weeks 8, 16, 24 and 48

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	9	1	72
Units: Subjects				
Baseline	0	0	0	0
Week 8	0	0	0	0
Week 16	0	0	0	1
Week 24	0	0	0	0
Week 48	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Findings in Weight Measurement, Counted as an AE

End point title	Number of Subjects With Clinically Significant Findings in Weight Measurement, Counted as an AE

End point description:

The number of subjects with clinically significant findings in weight measurement and were counted as an AE in the study were reported in this outcome measure. Safety analysis set: all subjects treated with tanezumab or placebo SC, including subjects received tanezumab 10 mg prior to protocol amendment 3.

End point type	Secondary

End point timeframe:

Day 1 of dosing up to maximum of Week 48

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	9	1	72
Units: Subjects	2	0	0	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormal Physical Examination at Screening

End point title	Number of Subjects With Abnormal Physical Examination at Screening

End point description:

Physical examination included assessment of general, head, eyes, ears, nose, neck, thyroid, lungs, heart, abdomen, extremities, skin, throat and other. Investigator judged abnormality in physical examinations. Safety analysis set: all subjects treated with tanezumab or placebo SC, including subjects received tanezumab 10 mg prior to protocol amendment 3. N:subjects evaluable for endpoint. n:subjects evaluable at specified assessments.

End point type	Secondary

End point timeframe:

Screening (up to 37 days prior to Day 1)

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	9	1	72
Units: Subjects				
General	3	1	0	6
Head	2	1	0	1
Eyes	4	1	0	1
Ears	1	0	0	1
Nose	0	0	0	0
Neck	2	1	0	2
Thyroid	2	0	0	0
Lungs	5	1	0	3

Heart	2	2	0	3
Abdomen	2	1	1	5
Extremities	14	0	0	10
Skin	15	2	0	10
Throat	3	1	0	2
Other 1	9	3	0	6
Other 2	1	3	0	2
Other 3	0	1	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Individual Adjudicated Joint Safety Outcome/Event

End point title	Number of Subjects With Individual Adjudicated Joint Safety Outcome/Event

End point description:

Joint-related safety events resulting in total joint replacement and/or discontinuation from the study as well as adverse events were reviewed by the External Adjudication Committee to confirm the potential events as adjudicated join safety event. In this endpoint, number of subjects with any of the joint safety adjudication outcomes of primary osteonecrosis, rapidly progressive osteoarthritis (OA) (type 1 and type 2), subchondral insufficiency fracture (or SPONK), or pathological fracture were reported. Other adjudication outcomes included normal progression of OA and other joint outcome. Safety analysis set was analysed. N:subjects evaluable for endpoint. n:subjects evaluable at specified assessments. In reporting arm, "Tanezumab10/20 mg" the subject did not have potential joint related safety event for analysis by Adjudication Committee.

End point type	Secondary

End point timeframe:

During the study, maximum up to Week 48

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	1	0[13]	3
Units: Subjects				
Rapidly Progressive OA	0	0		0
Rapidly Progressive OA type 1	0	0		0
Rapidly Progressive OA type 2	0	0		0
Primary Osteonecrosis	0	0		0
Pathological Fracture	0	0		2
Subchondral Insufficiency Fracture	0	0		0
Normal Progression of OA	0	0		0
Other Joint Outcome	1	1		1

Notes:

[13] - No subjects met criteria for data collection and analysis for 10/20 mg for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With At Least 1 Total Joint Replacements (TJR)

End point title	Number of Subjects With At Least 1 Total Joint Replacements (TJR)

End point description:

Number of subjects with joint replacement surgery were reported. The safety analysis set included all subjects treated with tanezumab or placebo SC, including subjects who received tanezumab 10 mg prior to protocol amendment 3.

End point type	Secondary

End point timeframe:

During the study, maximum up to Week 48

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	9	1	72
Units: Subjects	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Anti-Drug Antibodies (ADA) and Neutralising Anti-Drug Antibodies (NAb)

End point title	Number of Subjects With Anti-Drug Antibodies (ADA) and Neutralising Anti-Drug Antibodies (NAb)

End point description:

Human serum ADA samples were analysed for the presence or absence of anti-tanezumab antibodies by using a semi quantitative enzyme linked immunosorbent assay (ELISA). Number of subjects with presence of anti-tanezumab antibodies and neutralising anti-drug antibodies are reported. The safety analysis set included all subjects treated with tanezumab or placebo SC, including subjects who received tanezumab 10 mg prior to protocol amendment 3.

End point type	Secondary

End point timeframe:

Baseline (Day 1, before dosing) up to Week 48

End point values	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg	Tanezumab 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	9	1	72
Units: Subjects				
ADA	0	0	0	1
NAb	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 of dosing up to 24 weeks post last dose (maximum up to Week 48)	
Adverse event reporting additional description:	
Same event may appear as AE and SAE, what is presented are distinct events. Event may be categorised as serious in 1 subject and as non-serious in another subject or 1 subject may have experienced both serious and non-serious event during study. Safety analysis set was evaluated.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matched to tanezumab SC once every 8 weeks for 24 weeks.	
Reporting group title	Tanezumab 10 mg
Reporting group description:	
Subjects in this discontinued treatment arm, received tanezumab 10 mg SC once every 8 weeks before protocol amendment 3 and completed their treatment before the amendment.	
Reporting group title	Tanezumab 10/20 mg
Reporting group description:	
Subjects in this treatment group had received tanezumab 10 mg SC once every 8 weeks before protocol amendment 3 and after the amendment they continued remaining treatment with tanezumab 20 mg SC once every 8 weeks.	
Reporting group title	Tanezumab 20 mg
Reporting group description:	
Subjects received tanezumab 20 mg SC once every 8 weeks for 24 weeks.	

Serious adverse events	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 73 (38.36%)	2 / 9 (22.22%)	1 / 1 (100.00%)
number of deaths (all causes)	3	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder neoplasm			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (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
Breast cancer			

subjects affected / exposed	5 / 73 (6.85%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer metastatic			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	2 / 73 (2.74%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal cancer			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (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
Laryngeal cancer			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (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
Lung neoplasm malignant			
subjects affected / exposed	2 / 73 (2.74%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to bone			

subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (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
Metastases to central nervous system			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Metastases to meninges			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (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
Neoplasm prostate			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (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
Pancreatic carcinoma			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic neoplasm			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	7 / 73 (9.59%)	1 / 9 (11.11%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 7	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (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
Pyrexia			
subjects affected / exposed	0 / 73 (0.00%)	1 / 9 (11.11%)	0 / 1 (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
Respiratory, thoracic and mediastinal disorders			
Bronchitis chronic			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (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
Radius fracture			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (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
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular insufficiency			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			

subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (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
Paraparesis			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (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
Radiculopathy			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 73 (4.11%)	0 / 9 (0.00%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 73 (0.00%)	1 / 9 (11.11%)	0 / 1 (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

Flatulence			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (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
Vomiting			
subjects affected / exposed	0 / 73 (0.00%)	1 / 9 (11.11%)	0 / 1 (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
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (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
Osteonecrosis of jaw			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			

subjects affected / exposed	0 / 73 (0.00%)	1 / 9 (11.11%)	0 / 1 (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
Infections and infestations			
Pneumonia			
subjects affected / exposed	3 / 73 (4.11%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypophagia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Tanezumab 20 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	39 / 72 (54.17%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder neoplasm			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	3 / 72 (4.17%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Breast cancer metastatic			

subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cancer pain				
subjects affected / exposed	0 / 72 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colon cancer				
subjects affected / exposed	2 / 72 (2.78%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Colorectal cancer				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric cancer				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Laryngeal cancer				
subjects affected / exposed	0 / 72 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung neoplasm malignant				
subjects affected / exposed	4 / 72 (5.56%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Metastases to bone				
subjects affected / exposed	3 / 72 (4.17%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Metastases to central nervous system				

subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Metastases to meninges				
subjects affected / exposed	0 / 72 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neoplasm prostate				
subjects affected / exposed	0 / 72 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatic carcinoma				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatic neoplasm				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	7 / 72 (9.72%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Tumour pain				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Deep vein thrombosis				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral ischaemia				

subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gait disturbance			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Bronchitis chronic			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pleurisy			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	2 / 72 (2.78%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			

subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Radius fracture			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Cerebrovascular insufficiency			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Paraparesis				
subjects affected / exposed	2 / 72 (2.78%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Radiculopathy				
subjects affected / exposed	0 / 72 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	3 / 72 (4.17%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	0 / 72 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Vertigo				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 72 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Flatulence				

subjects affected / exposed	0 / 72 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Jaundice				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Haematuria				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				
subjects affected / exposed	0 / 72 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteonecrosis of jaw				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pathological fracture				
subjects affected / exposed	0 / 72 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypophagia			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Placebo	Tanezumab 10 mg	Tanezumab 10/20 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 73 (58.90%)	8 / 9 (88.89%)	1 / 1 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Breast cancer			
subjects affected / exposed	2 / 73 (2.74%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Malignant neoplasm progression			
subjects affected / exposed	0 / 73 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Metastases to bone			
subjects affected / exposed	0 / 73 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Neoplasm			

subjects affected / exposed	0 / 73 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Prostate cancer			
subjects affected / exposed	2 / 73 (2.74%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Lymphoedema			
subjects affected / exposed	2 / 73 (2.74%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Orthostatic hypotension			
subjects affected / exposed	1 / 73 (1.37%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Pallor			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 73 (5.48%)	0 / 9 (0.00%)	1 / 1 (100.00%)
occurrences (all)	4	0	1
Fatigue			
subjects affected / exposed	5 / 73 (6.85%)	1 / 9 (11.11%)	1 / 1 (100.00%)
occurrences (all)	7	5	1
Influenza like illness			
subjects affected / exposed	1 / 73 (1.37%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Pain			
subjects affected / exposed	3 / 73 (4.11%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Oedema peripheral			
subjects affected / exposed	2 / 73 (2.74%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Peripheral swelling			

subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	2 / 73 (2.74%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	0 / 73 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 73 (2.74%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Dyspnoea			
subjects affected / exposed	3 / 73 (4.11%)	2 / 9 (22.22%)	0 / 1 (0.00%)
occurrences (all)	3	2	0
Oropharyngeal pain			
subjects affected / exposed	2 / 73 (2.74%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Pulmonary mass			
subjects affected / exposed	0 / 73 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	0 / 73 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 73 (4.11%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Depression			
subjects affected / exposed	2 / 73 (2.74%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Depressed mood			
subjects affected / exposed	3 / 73 (4.11%)	0 / 9 (0.00%)	1 / 1 (100.00%)
occurrences (all)	5	0	1
Insomnia			

subjects affected / exposed	1 / 73 (1.37%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 73 (2.74%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Weight decreased			
subjects affected / exposed	3 / 73 (4.11%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
White blood cell count decreased			
subjects affected / exposed	2 / 73 (2.74%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	6	0	0
Weight increased			
subjects affected / exposed	0 / 73 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	3 / 73 (4.11%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Toxicity to various agents			
subjects affected / exposed	0 / 73 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 73 (4.11%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Headache			
subjects affected / exposed	2 / 73 (2.74%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Neuralgia			
subjects affected / exposed	2 / 73 (2.74%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Paraesthesia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Somnolence			

subjects affected / exposed	2 / 73 (2.74%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	9 / 73 (12.33%)	1 / 9 (11.11%)	1 / 1 (100.00%)
occurrences (all)	9	1	2
Leukopenia			
subjects affected / exposed	3 / 73 (4.11%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 73 (1.37%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Eye disorders			
Visual acuity reduced			
subjects affected / exposed	0 / 73 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 73 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	3 / 73 (4.11%)	2 / 9 (22.22%)	1 / 1 (100.00%)
occurrences (all)	3	2	1
Diarrhoea			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	2 / 73 (2.74%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Gastritis			
subjects affected / exposed	1 / 73 (1.37%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Nausea			
subjects affected / exposed	6 / 73 (8.22%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	8	0	0
Toothache			

subjects affected / exposed	4 / 73 (5.48%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	5	0	0
Vomiting			
subjects affected / exposed	6 / 73 (8.22%)	0 / 9 (0.00%)	1 / 1 (100.00%)
occurrences (all)	7	0	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 73 (4.11%)	2 / 9 (22.22%)	0 / 1 (0.00%)
occurrences (all)	3	2	0
Decubitus ulcer			
subjects affected / exposed	2 / 73 (2.74%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Rash			
subjects affected / exposed	4 / 73 (5.48%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	2 / 73 (2.74%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Urinary incontinence			
subjects affected / exposed	2 / 73 (2.74%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	9 / 73 (12.33%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	14	1	0
Arthralgia			
subjects affected / exposed	7 / 73 (9.59%)	2 / 9 (22.22%)	0 / 1 (0.00%)
occurrences (all)	18	2	0
Myalgia			
subjects affected / exposed	1 / 73 (1.37%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Osteoarthritis			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			

subjects affected / exposed	5 / 73 (6.85%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	6	0	0
Pathological fracture			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bacterial infection			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	2 / 73 (2.74%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Gastroenteritis			
subjects affected / exposed	0 / 73 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Oral candidiasis			
subjects affected / exposed	0 / 73 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 73 (1.37%)	0 / 9 (0.00%)	1 / 1 (100.00%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 73 (5.48%)	1 / 9 (11.11%)	1 / 1 (100.00%)
occurrences (all)	5	1	2
Dehydration			

subjects affected / exposed	0 / 73 (0.00%)	0 / 9 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Hypocalcaemia			
subjects affected / exposed	3 / 73 (4.11%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Hypokalaemia			
subjects affected / exposed	3 / 73 (4.11%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Hypomagnesaemia			
subjects affected / exposed	2 / 73 (2.74%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	Tanezumab 20 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 72 (68.06%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	2 / 72 (2.78%)		
occurrences (all)	3		
Breast cancer			
subjects affected / exposed	4 / 72 (5.56%)		
occurrences (all)	5		
Malignant neoplasm progression			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences (all)	1		
Metastases to bone			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences (all)	2		
Neoplasm			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences (all)	0		
Prostate cancer			
subjects affected / exposed	3 / 72 (4.17%)		
occurrences (all)	3		
Vascular disorders			

Hypertension			
subjects affected / exposed	2 / 72 (2.78%)		
occurrences (all)	2		
Lymphoedema			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences (all)	0		
Orthostatic hypotension			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences (all)	1		
Pallor			
subjects affected / exposed	2 / 72 (2.78%)		
occurrences (all)	2		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	6 / 72 (8.33%)		
occurrences (all)	9		
Fatigue			
subjects affected / exposed	6 / 72 (8.33%)		
occurrences (all)	6		
Influenza like illness			
subjects affected / exposed	4 / 72 (5.56%)		
occurrences (all)	5		
Pain			
subjects affected / exposed	6 / 72 (8.33%)		
occurrences (all)	8		
Oedema peripheral			
subjects affected / exposed	9 / 72 (12.50%)		
occurrences (all)	9		
Peripheral swelling			
subjects affected / exposed	2 / 72 (2.78%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	2 / 72 (2.78%)		
occurrences (all)	2		
Immune system disorders			

Contrast media allergy subjects affected / exposed occurrences (all)	0 / 72 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Pulmonary mass subjects affected / exposed occurrences (all) Wheezing subjects affected / exposed occurrences (all)	 2 / 72 (2.78%) 2 3 / 72 (4.17%) 5 0 / 72 (0.00%) 0 0 / 72 (0.00%) 0 0 / 72 (0.00%) 0		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all) Depressed mood subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	 0 / 72 (0.00%) 0 2 / 72 (2.78%) 2 2 / 72 (2.78%) 5 5 / 72 (6.94%) 5		
Investigations Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	 0 / 72 (0.00%) 0		

Weight decreased subjects affected / exposed occurrences (all)	3 / 72 (4.17%) 3		
White blood cell count decreased subjects affected / exposed occurrences (all)	0 / 72 (0.00%) 0		
Weight increased subjects affected / exposed occurrences (all)	0 / 72 (0.00%) 0		
Injury, poisoning and procedural complications			
Fall subjects affected / exposed occurrences (all)	5 / 72 (6.94%) 7		
Toxicity to various agents subjects affected / exposed occurrences (all)	0 / 72 (0.00%) 0		
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	3 / 72 (4.17%) 4		
Headache subjects affected / exposed occurrences (all)	5 / 72 (6.94%) 5		
Neuralgia subjects affected / exposed occurrences (all)	2 / 72 (2.78%) 3		
Paraesthesia subjects affected / exposed occurrences (all)	2 / 72 (2.78%) 6		
Somnolence subjects affected / exposed occurrences (all)	2 / 72 (2.78%) 2		
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	9 / 72 (12.50%) 10		

Leukopenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all)	2 / 72 (2.78%) 2 0 / 72 (0.00%) 0		
Eye disorders Visual acuity reduced subjects affected / exposed occurrences (all)	0 / 72 (0.00%) 0		
Gastrointestinal disorders Abdominal hernia subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Gastritis subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	0 / 72 (0.00%) 0 6 / 72 (8.33%) 6 6 / 72 (8.33%) 7 1 / 72 (1.39%) 3 0 / 72 (0.00%) 0 4 / 72 (5.56%) 7 0 / 72 (0.00%) 0 4 / 72 (5.56%) 5		
Skin and subcutaneous tissue disorders			

Pruritus			
subjects affected / exposed	2 / 72 (2.78%)		
occurrences (all)	3		
Decubitus ulcer			
subjects affected / exposed	2 / 72 (2.78%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences (all)	1		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences (all)	0		
Urinary incontinence			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences (all)	2		
Arthralgia			
subjects affected / exposed	11 / 72 (15.28%)		
occurrences (all)	16		
Myalgia			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences (all)	0		
Osteoarthritis			
subjects affected / exposed	2 / 72 (2.78%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	3 / 72 (4.17%)		
occurrences (all)	4		
Pathological fracture			
subjects affected / exposed	3 / 72 (4.17%)		
occurrences (all)	3		
Infections and infestations			

Bacterial infection			
subjects affected / exposed	2 / 72 (2.78%)		
occurrences (all)	2		
Bronchitis			
subjects affected / exposed	2 / 72 (2.78%)		
occurrences (all)	2		
Cystitis			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	4 / 72 (5.56%)		
occurrences (all)	4		
Oral candidiasis			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	3 / 72 (4.17%)		
occurrences (all)	3		
Urinary tract infection			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	10 / 72 (13.89%)		
occurrences (all)	10		
Dehydration			
subjects affected / exposed	2 / 72 (2.78%)		
occurrences (all)	2		
Hypocalcaemia			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences (all)	0		
Hypokalaemia			

subjects affected / exposed	1 / 72 (1.39%)		
occurrences (all)	1		
Hypomagnesaemia			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 February 2017	To provide background and rationale for key changes

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported