Clinical trial results:
A Phase 3, Randomized, Double Blind, Placebo and Active-Controlled, Multicenter, Parallel-Group Study of the Analgesic Efficacy and Safety of Tanezumab in Adult Subjects with Chronic low Back Pain

Summary

EudraCT number	2012-005495-34
Trial protocol	SE HU DK ES
Global end of trial date	20 December 2018

Results information

Result version number	v2 (current)
This version publication date	06 June 2020
First version publication date	04 January 2020
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	A4091059

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02528253
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 18007181021, 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)	
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	20 December 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Demonstrate superior analgesic efficacy of tanezumab 10 mg and 5 mg administered subcutaneously (SC) every 8 weeks compared to placebo at Week 16.

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 trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 August 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 80
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Hungary: 24
Country: Number of subjects enrolled	Japan: 129
Country: Number of subjects enrolled	Korea, Republic of: 16
Country: Number of subjects enrolled	Spain: 61
Country: Number of subjects enrolled	Sweden: 11
Country: Number of subjects enrolled	United States: 1503
Worldwide total number of subjects	1825
EEA total number of subjects	97

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)	1607
From 65 to 84 years	218
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 1832 subjects were enrolled in the study, however, only those subjects were included in subject disposition section who received at least 1 dose of study drug.

Pre-assignment

Screening details:

Treatment period was up to Week 56. Safety follow up period started at Week 64, thus Weeks 64 and 80 time points were during safety follow up period. Percentage (%) reduction in low back pain intensity (LBPI) and participants global assessment (PGA) 2-point reduction are efficacy measures and not applicable during safety follow up.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo Followed by Tanezumab 5 mg

Arm description:

Placebo matched to tanezumab (RN624 or PF-04383119) injection administered subcutaneously (SC) once every 8 weeks and placebo tablets matched to tramadol prolonged release (PR), orally, once daily from Day 1 (baseline) up to week 16. At week 16, subjects who met efficacy responder criteria (greater than equal to [>=] 30 percent [%] reduction in average LBPI score and >=15% reduction in average LBPI score relative to baseline at any week from week 1 to week 15), then received tanezumab 5 milligram (mg), SC, once every 8 weeks plus placebo tablets matched to tramadol PR, orally, once daily from week 16 to week 56.

Arm type	Experimental
Investigational medicinal product name	Tanezumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subject received tanezumab injection administered subcutaneously (SC) once every 8 weeks from Day 1.

Arm title	Placebo Followed by Tanezumab 10 mg

Arm description:

Placebo matched to tanezumab (RN624 or PF-04383119) injection administered SC, once every 8 weeks and placebo tablets matched to tramadol PR, orally, once daily from Day 1 (baseline) up to week 16. At week 16, subjects who met efficacy responder criteria, then received tanezumab 10 mg, SC, once every 8 weeks plus placebo tablets matched to tramadol PR, orally, once daily from week 16 to week 56.

Arm type	Experimental
Investigational medicinal product name	Tanezumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subject received tanezumab injection administered subcutaneously (SC) once every 8 weeks from Day 1.

Arm title	Tanezumab 5 mg

Arm description:

Tanezumab (RN624 or PF-04383119) 5 mg injection administered SC once every 8 weeks and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 56.

Arm type	Experimental
Investigational medicinal product name	Tanezumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subject received tanezumab injection administered subcutaneously (SC) once every 8 weeks from Day 1.

Arm title	Tanezumab 10 mg

Arm description:

Tanezumab (RN624 or PF-04383119) 10 mg injection administered SC once every 8 weeks and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 56.

Arm type	Experimental
Investigational medicinal product name	Tanezumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subject received tanezumab injection administered subcutaneously (SC) once every 8 weeks from Day 1.

Arm title	Tramadol

Arm description:

Tramadol PR tablet of 100 mg (during baseline to week 4, dose increments by 100 mg was allowed up to a maximum of 300 mg, depending on pain relief or tolerability), once daily and placebo injection matched to tramadol, administered SC once every 8 weeks, from Day 1 up to week 56.

Arm type	Experimental
Investigational medicinal product name	Tramadol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subject received tramadol tablet administered orally once daily.

Number of subjects in period 1	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg
Started	205	204	407
Completed	130	134	267
Not completed	75	70	140
Adverse event, serious fatal	2	2	1
Withdrawn Due to Pregnancy	-	1	-
Consent withdrawn by subject	25	20	29

Adverse event, non-fatal	3	4	4
Unspecified	21	22	58
Lost to follow-up	16	9	31
Insufficient clinical response	7	10	13
Protocol deviation	1	2	4

Number of subjects in period 1	Tanezumab 10 mg	Tramadol
Started	407	602
Completed	271	379
Not completed	136	223
Adverse event, serious fatal	-	1
Withdrawn Due to Pregnancy	-	1
Consent withdrawn by subject	48	73
Adverse event, non-fatal	8	18
Unspecified	52	76
Lost to follow-up	16	34
Insufficient clinical response	12	16
Protocol deviation	-	4

Baseline characteristics

Reporting groups	
Reporting group title	Placebo Followed by Tanezumab 5 mg
Reporting group description:	
Placebo matched to tanezumab (RN624 or PF-04383119) injection administered subcutaneously (SC) once every 8 weeks and placebo tablets matched to tramadol prolonged release (PR), orally, once daily from Day 1 (baseline) up to week 16. At week 16, subjects who met efficacy responder criteria (greater than equal to [>=] 30 percent [%] reduction in average LBPI score and >=15% reduction in average LBPI score relative to baseline at any week from week 1 to week 15), then received tanezumab 5 milligram (mg), SC, once every 8 weeks plus placebo tablets matched to tramadol PR, orally, once daily from week 16 to week 56.	
Reporting group title	Placebo Followed by Tanezumab 10 mg
Reporting group description:	
Placebo matched to tanezumab (RN624 or PF-04383119) injection administered SC, once every 8 weeks and placebo tablets matched to tramadol PR, orally, once daily from Day 1 (baseline) up to week 16. At week 16, subjects who met efficacy responder criteria, then received tanezumab 10 mg, SC, once every 8 weeks plus placebo tablets matched to tramadol PR, orally, once daily from week 16 to week 56.	
Reporting group title	Tanezumab 5 mg
Reporting group description:	
Tanezumab (RN624 or PF-04383119) 5 mg injection administered SC once every 8 weeks and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 56.	
Reporting group title	Tanezumab 10 mg
Reporting group description:	
Tanezumab (RN624 or PF-04383119) 10 mg injection administered SC once every 8 weeks and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 56.	
Reporting group title	Tramadol
Reporting group description:	
Tramadol PR tablet of 100 mg (during baseline to week 4, dose increments by 100 mg was allowed up to a maximum of 300 mg, depending on pain relief or tolerability), once daily and placebo injection matched to tramadol, administered SC once every 8 weeks, from Day 1 up to week 56.	

Reporting group values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg
Number of subjects	205	204	407
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	178	186	362
From 65-84 years	27	18	45
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	49.01	48.97	48.66
standard deviation	± 13.76	± 12.00	± 12.36

Sex: Female, Male Units: Subjects			
Female	123	113	248
Male	82	91	159
Race/Ethnicity, Customized Units: Subjects			
White	154	142	295
Black or African American	35	35	65
Asian	13	25	39
Other	3	2	8

Reporting group values	Tanezumab 10 mg	Tramadol	Total
Number of subjects	407	602	1825
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	355	526	1607
From 65-84 years	52	76	218
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	49.15	48.42	
standard deviation	± 12.36	± 13.08	-
Sex: Female, Male Units: Subjects			
Female	218	339	1041
Male	189	263	784
Race/Ethnicity, Customized Units: Subjects			
White	303	428	1322
Black or African American	66	102	303
Asian	28	65	170
Other	10	7	30

End points reporting groups

Reporting group title	Placebo Followed by Tanezumab 5 mg

Reporting group description:

Placebo matched to tanezumab (RN624 or PF-04383119) injection administered subcutaneously (SC) once every 8 weeks and placebo tablets matched to tramadol prolonged release (PR), orally, once daily from Day 1 (baseline) up to week 16. At week 16, subjects who met efficacy responder criteria (greater than equal to [>=] 30 percent [%] reduction in average LBPI score and >=15% reduction in average LBPI score relative to baseline at any week from week 1 to week 15), then received tanezumab 5 milligram (mg), SC, once every 8 weeks plus placebo tablets matched to tramadol PR, orally, once daily from week 16 to week 56.

Reporting group title	Placebo Followed by Tanezumab 10 mg

Reporting group description:

Placebo matched to tanezumab (RN624 or PF-04383119) injection administered SC, once every 8 weeks and placebo tablets matched to tramadol PR, orally, once daily from Day 1 (baseline) up to week 16. At week 16, subjects who met efficacy responder criteria, then received tanezumab 10 mg, SC, once every 8 weeks plus placebo tablets matched to tramadol PR, orally, once daily from week 16 to week 56.

Reporting group title	Tanezumab 5 mg

Reporting group description:

Tanezumab (RN624 or PF-04383119) 5 mg injection administered SC once every 8 weeks and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 56.

Reporting group title	Tanezumab 10 mg

Reporting group description:

Tanezumab (RN624 or PF-04383119) 10 mg injection administered SC once every 8 weeks and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 56.

Reporting group title	Tramadol

Reporting group description:

Tramadol PR tablet of 100 mg (during baseline to week 4, dose increments by 100 mg was allowed up to a maximum of 300 mg, depending on pain relief or tolerability), once daily and placebo injection matched to tramadol, administered SC once every 8 weeks, from Day 1 up to week 56.

Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Placebo matched to tanezumab (RN624 or PF-04383119) injection administered SC once every 8 weeks from Day 1 (baseline), and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 16. At week 16, subjects who met efficacy responder criteria (>=30 percentage % reduction in average LBPI score and >=15% reduction in average LBPI score relative to baseline at any week from week 1 to week 15), then received tanezumab 5 mg or 10 mg, SC, once every 8 weeks plus placebo tablets matched to tramadol PR, orally, once daily from week 16 to week 56.

Subject analysis set title	Tramadol PR
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Tramadol PR tablet of 100 mg (during baseline to week 4, dose increments by 100 mg was allowed up to a maximum of 300 mg, depending on pain relief or tolerability), once daily and placebo injection matched to tramadol, administered SC once every 8 weeks, from Day 1 up to week 16.

Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Placebo matched to tanezumab (RN624 or PF-04383119) injection administered SC once every 8 weeks from Day 1 (baseline), and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 16. At week 16, subjects who met efficacy responder criteria (>=30 percentage % reduction in average LBPI score and >=15% reduction in average LBPI score relative to baseline at any week from week 1 to week 15), then received tanezumab 5 mg or 10 mg, SC, once every 8 weeks plus placebo tablets matched to tramadol PR, orally, once daily from week 16 to week 56.

Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Placebo matched to tanezumab (RN624 or PF-04383119) injection administered SC once every 8 weeks from Day 1 (baseline), and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 16. At week 16, subjects who met efficacy responder criteria (>=30 percentage % reduction in average LBPI score and >=15% reduction in average LBPI score relative to baseline at any week from week 1 to week 15), then received tanezumab 5 mg or 10 mg, SC, once every 8 weeks plus placebo tablets matched to tramadol PR, orally, once daily from week 16 to week 56.

Subject analysis set title	Tramadol PR
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Tramadol PR tablet of 100 mg (during baseline to week 4, dose increments by 100 mg was allowed up to a maximum of 300 mg, depending on pain relief or tolerability), once daily and placebo injection matched to tramadol, administered SC once every 8 weeks, from Day 1 up to week 56.

Subject analysis set title	Tramadol PR
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Tramadol PR tablet of 100 mg (during baseline to week 4, dose increments by 100 mg was allowed up to a maximum of 300 mg, depending on pain relief or tolerability), once daily and placebo injection matched to tramadol, administered SC once every 8 weeks, from Day 1 up to week 56.

Subject analysis set title	Tramadol PR
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Tramadol PR tablet of 100 mg (during baseline to week 4, dose increments by 100 mg was allowed up to a maximum of 300 mg, depending on pain relief or tolerability), once daily and placebo injection matched to tramadol, administered SC once every 8 weeks, from Day 1 up to week 56.

Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Placebo matched to tanezumab (RN624 or PF-04383119) injection administered SC, once every 8 weeks from Day 1 (baseline), and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 16.

Subject analysis set title	Tanezumab 5 mg Pooled
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Placebo matched to tanezumab (RN624 or PF-04383119) injection administered SC, once every 8 weeks from Day 1 (baseline), and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 16. At week 16, subjects who met efficacy responder criteria (>=30 % reduction in average LBPI score and >=15% reduction in average LBPI score relative to baseline at any week from week 1 to week 15), then received tanezumab 5 mg or 10 mg, SC, once every 8 weeks plus placebo tablets matched to tramadol PR, orally, once daily, from week 16 to week 56.Those subjects were also included who received tanezumab 5 mg injection administered SC once every 8 weeks from Day 1 and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 56.

Subject analysis set title	Tanezumab 10 mg Pooled
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Placebo matched to tanezumab (RN624 or PF-04383119) injection administered SC, once every 8 weeks from Day 1 (baseline), and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 16. At week 16, subjects who met efficacy responder criteria (>=30 % reduction in average LBPI score and >=15% reduction in average LBPI score relative to baseline at any week from week 1 to week 15), then received tanezumab 5 mg or 10 mg, SC, once every 8 weeks plus placebo tablets matched to tramadol PR, orally, once daily, from week 16 to week 56.Those subjects were also included who received tanezumab 10 mg injection administered SC once every 8 weeks from Day 1 and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 56.

Subject analysis set title	Tramadol PR
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Tramadol PR tablet of 100 mg (during baseline to week 4, dose increments by 100 mg was allowed up to a maximum of 300 mg, depending on pain relief or tolerability), once daily and placebo injection matched to tramadol, administered SC once every 8 weeks, from Day 1 up to week 56.

Subject analysis set title	Placebo

Subject analysis set type	Intention-to-treat

Subject analysis set description:

Placebo matched to tanezumab (RN624 or PF-04383119) injection administered SC, once every 8 weeks from Day 1 (baseline), and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 16.

Subject analysis set title	Tanezumab 10 mg Pooled
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Placebo matched to tanezumab (RN624 or PF-04383119) injection administered SC, once every 8 weeks from Day 1 (baseline), and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 16. At week 16, subjects who met efficacy responder criteria (>=30 % reduction in average LBPI score and >=15% reduction in average LBPI score relative to baseline at any week from week 1 to week 15), then received tanezumab 5 mg or 10 mg, SC, once every 8 weeks plus placebo tablets matched to tramadol PR, orally, once daily, from week 16 to week 56.Those subjects were also included who received tanezumab 10 mg injection administered SC once every 8 weeks from Day 1 and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 56.

Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Placebo matched to tanezumab (RN624 or PF-04383119) injection administered SC once every 8 weeks from Day 1 (baseline), and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 16. At week 16, subjects who met efficacy responder criteria (>=30 percentage % reduction in average LBPI score and >=15% reduction in average LBPI score relative to baseline at any week from week 1 to week 15), then received tanezumab 5 mg or 10 mg, SC, once every 8 weeks plus placebo tablets matched to tramadol PR, orally, once daily from week 16 to week 56.

Subject analysis set title	Tanezumab 5 mg Pooled
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Placebo matched to tanezumab (RN624 or PF-04383119) injection administered SC, once every 8 weeks from Day 1 (baseline), and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 16. At week 16, subjects who met efficacy responder criteria (>=30 % reduction in average LBPI score and >=15% reduction in average LBPI score relative to baseline at any week from week 1 to week 15), then received tanezumab 5 mg or 10 mg, SC, once every 8 weeks plus placebo tablets matched to tramadol PR, orally, once daily, from week 16 to week 56.Those subjects were also included who received tanezumab 5 mg injection administered SC once every 8 weeks from Day 1 and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 56.

Subject analysis set title	Tanezumab 10 mg Pooled
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Placebo matched to tanezumab (RN624 or PF-04383119) injection administered SC, once every 8 weeks from Day 1 (baseline), and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 16. At week 16, subjects who met efficacy responder criteria (>=30 % reduction in average LBPI score and >=15% reduction in average LBPI score relative to baseline at any week from week 1 to week 15), then received tanezumab 5 mg or 10 mg, SC, once every 8 weeks plus placebo tablets matched to tramadol PR, orally, once daily, from week 16 to week 56. Those subjects were also included who received tanezumab 10 mg injection administered SC once every 8 weeks from Day 1 and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 56.

Subject analysis set title	Pooled Placebo
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Placebo matched to tanezumab (RN624 or PF-04383119) injection administered SC, once every 8 weeks from Day 1 (baseline), and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 16. At week 16, subjects who met efficacy responder criteria (>=30 % reduction in average LBPI score and >=15% reduction in average LBPI score relative to baseline at any week from week 1 to week 15), then received tanezumab 5 mg or 10 mg, SC, once every 8 weeks plus placebo tablets matched to tramadol PR, orally, once daily, from week 16 to week 56.

Primary: Change From Baseline in Daily Average Low Back Pain Intensity (LBPI) Score for Tanezumab Versus (Vs) Placebo at Week 16

End point title	Change From Baseline in Daily Average Low Back Pain Intensity (LBPI) Score for Tanezumab Versus (Vs) Placebo at Week 16[1]

End point description:

Average low back pain was assessed on an 11-point numeric rating scale (NRS) captured through an interactive response technology (IRT). Subjects described their average low back pain during the past 24 hours on a scale ranging from 0 (no pain) to 10 (worst possible pain), where higher scores indicated higher pain. ITT population: randomised subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo).Pre-specified intent of study for efficacy data up to W16 was to analyze subjects who received placebo from Day1 and then received tanezumab 5/10 mg at W16,together,in placebo arm.Data has been reported per four arms.

End point type	Primary

End point timeframe:

Baseline, Week 16

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: units on a scale				
least squares mean (standard error)	-2.98 (± 0.14)	-3.08 (± 0.14)	-2.68 (± 0.15)	-2.81 (± 0.12)

Statistical analyses

Statistical analysis title	Pooled Placebo Versus Tanezumab 5 mg

Statistical analysis description:

Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. Analysis of covariance (ANCOVA) model for imputed datasets included treatment as a fixed effect, and baseline average low back pain intensity (LBPI) as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1117
Method	ANCOVA
Parameter estimate	Least Square (LS) Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	0.07
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Pooled Placebo Versus Tanezumab 10 mg

Statistical analysis description:

Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0281
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	-0.04
Variability estimate	Standard error of the mean
Dispersion value	0.18

Secondary: Change From Baseline in Roland Morris Disability Questionnaire (RMDQ) at Week 16 for Tanezumab Versus (Vs) Placebo

End point title	Change From Baseline in Roland Morris Disability Questionnaire (RMDQ) at Week 16 for Tanezumab Versus (Vs) Placebo[2]

End point description:

The RMDQ is a self-administered, widely used health status measure index of how well subjects with low back pain (LBP) are able to function with regard to daily activities. It measures pain and function, using 24 items describing limitations to everyday life that can be caused by LBP. The score of the RMDQ is the total number of items checked ranging from 0 (no disability) to 24 (maximum disability), where higher scores indicated greater disability. ITT population was analysed. Pre-specified intent of study for efficacy data up to W16 was to analyze subjects who received placebo from Day1 and then received tanezumab 5/10 mg at W16,together,in placebo arm.Data has been reported per four arms.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: units on a scale				
least squares mean (standard error)	-6.27 (± 0.35)	-6.69 (± 0.35)	-4.95 (± 0.36)	-5.21 (± 0.30)

Statistical analyses

Statistical analysis title	Pooled Placebo Versus Tanezumab 5 mg
Statistical analysis description:	
Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.	
Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0035
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.21
upper limit	-0.43
Variability estimate	Standard error of the mean
Dispersion value	0.45

Statistical analysis title	Pooled Placebo Versus Tanezumab 10 mg
Statistical analysis description:	
Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.	
Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0002
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.64
upper limit	-0.83
Variability estimate	Standard error of the mean
Dispersion value	0.46

Secondary: Change From Baseline in Daily Average Low Back Pain Intensity (LBPI) Score for Tanezumab Versus (Vs) Tramadol at Week 16

End point title	Change From Baseline in Daily Average Low Back Pain Intensity (LBPI) Score for Tanezumab Versus (Vs) Tramadol at Week 16[3]

End point description:

Average LBP was assessed on an 11-point NRS captured through an IRT. Subjects described their average LBP during the past 24 hours on a scale ranging from 0 (no pain) to 10 (worst possible pain), where higher scores indicated higher pain. ITT population was analyzed.Pre-specified intent of study for efficacy data up to W16 was to analyze subjects who received placebo from Day1 and then received tanezumab 5/10 mg at W16,together,in placebo arm.Data has been reported per four arms.

End point type	Secondary

End point timeframe:

Baseline, Week 16

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: units on a scale				
least squares mean (standard error)	-2.98 (± 0.14)	-3.08 (± 0.14)	-2.68 (± 0.15)	-2.81 (± 0.12)

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3118
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.16
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0958
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.17

Secondary: Change From Baseline in Daily Average Low Back Pain Intensity (LBPI) Score at Weeks 2, 4, 8, 12, 24, 32, 40, 48 and 56

End point title	Change From Baseline in Daily Average Low Back Pain Intensity (LBPI) Score at Weeks 2, 4, 8, 12, 24, 32, 40, 48 and 56[4]

End point description:

ALBP was assessed on an 11-point NRS captured through an IRT.LBPI score was captured once daily from baseline up to w16, and once weekly from w16 to w64.Subjects described their average LBP during the past 24 hours on a scale ranging from 0 (no pain) to 10 (worst possible pain), where higher scores indicated higher pain.Pre-specified intent of study for efficacy data up to W16 was to analyze subjects who received placebo from Day1 & then received tan 5/10 mg at W16,together,in placebo arm.Data has been reported per four arms. ITT population.Data were not collected after W16 in placebo arm,as those who met criteria to continue,switched to active treatment with tan after W16.Pre-specified intent of study was to compare tan vs placebo for data up to & including W16 & comparisons of tan Vs tram for data up to & including W56.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 12, 24, 32, 40, 48 and 56

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: units on a scale				
least squares mean (standard error)				
Change at Week 2	-1.54 (± 0.09)	-1.59 (± 0.09)	-1.17 (± 0.09)	-1.36 (± 0.08)
Change at Week 4	-2.24 (± 0.12)	-2.43 (± 0.12)	-1.75 (± 0.12)	-1.99 (± 0.10)
Change at Week 8	-2.64 (± 0.13)	-2.79 (± 0.13)	-2.10 (± 0.13)	-2.43 (± 0.11)
Change at Week 12	-2.92 (± 0.13)	-3.12 (± 0.13)	-2.54 (± 0.13)	-2.74 (± 0.11)
Change at Week 24	-2.76 (± 0.16)	-2.92 (± 0.16)	99999 (± 99999)	-2.64 (± 0.14)
Change at Week 32	-2.74 (± 0.17)	-2.75 (± 0.16)	99999 (± 99999)	-2.52 (± 0.14)
Change at Week 40	-2.64 (± 0.17)	-2.67 (± 0.17)	99999 (± 99999)	-2.49 (± 0.14)
Change at Week 48	-2.58 (± 0.17)	-2.62 (± 0.17)	99999 (± 99999)	-2.43 (± 0.15)
Change at Week 56	-2.52 (± 0.17)	-2.62 (± 0.17)	99999 (± 99999)	-2.40 (± 0.15)

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo
Statistical analysis description:	
Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.	
Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0015
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	-0.14
Variability estimate	Standard error of the mean
Dispersion value	0.12

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo
Statistical analysis description:	
Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.	
Comparison groups	Tanezumab 10 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0004
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	-0.19
Variability estimate	Standard error of the mean
Dispersion value	0.12

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0771
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.41
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.11

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0959
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.39
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.11

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.037
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.44
upper limit	-0.01
Variability estimate	Standard error of the mean
Dispersion value	0.11

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0008
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.96
upper limit	-0.39
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR

Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0711
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.13

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0661
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.13

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0009
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	-0.18
Variability estimate	Standard error of the mean
Dispersion value	0.13

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0008
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.84
upper limit	-0.22
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	-0.38
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0274
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	-0.04
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1495
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.08
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0123
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	-0.08
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 12: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0307
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.71
upper limit	-0.03
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 12: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0009
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.91
upper limit	-0.24
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 12: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR

Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2103
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.51
upper limit	0.11
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 12: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2656
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	0.13
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 12: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0152
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.68
upper limit	-0.07
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5164
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.25
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1488
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2431
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.15
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2428
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	0.16
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4561
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	0.24
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3523
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4403
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0.23
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3205
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.58
upper limit	0.19
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5763
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.51
upper limit	0.28
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as a fixed effect, and baseline average LBPI as a covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2887
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	0.18
Variability estimate	Standard error of the mean
Dispersion value	0.2

Secondary: Change From Baseline in Daily Average Low Back Pain Intensity (LBPI) Score at Week 64

End point title	Change From Baseline in Daily Average Low Back Pain Intensity (LBPI) Score at Week 64[5]

End point description:

Average LBP was assessed on an 11-point NRS captured through an IRT. The LBPI score was captured once a week for week 64. Subjects described their average LBP during the past 24 hours on a scale ranging from 0 (no pain) to 10 (worst possible pain), where higher scores indicated higher pain. ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo). 'Number analyzed' (n) = subjects evaluable for this endpoint at specified time point.

End point type	Secondary

End point timeframe:

Baseline, Week 64

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 200, 204, 406, 406, 605)	7.16 (± 1.15)	7.23 (± 1.09)	7.25 (± 1.08)	7.18 (± 1.13)
Change at Week 64 (n= 58, 53, 126, 145, 176)	-4.36 (± 2.28)	-4.32 (± 2.01)	-4.04 (± 2.15)	-3.71 (± 2.39)

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: units on a scale				

arithmetic mean (standard deviation)				
Baseline (n= 200, 204, 406, 406, 605)	7.17 (± 1.16)			
Change at Week 64 (n= 58, 53, 126, 145, 176)	-4.08 (± 2.12)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Roland Morris Disability Questionnaire (RMDQ) Total Score at Weeks 2, 4, 8, 16 (for Tanezumab vs Tramadol) 24, 32, 40, 48 and 56

End point title	Change From Baseline in Roland Morris Disability Questionnaire (RMDQ) Total Score at Weeks 2, 4, 8, 16 (for Tanezumab vs Tramadol) 24, 32, 40, 48 and 56[6]

End point description:

RMDQ:self-administered,used health status measure index of how well subjects with LBP are able to function with regard to daily activities. It measures pain and function, using 24 items describing limitations to everyday life that can be caused by LBP. The total score of the RMDQ is the total number of items checked ranging from 0 (no disability) to 24 (maximum disability), where higher scores indicated greater disability. Pre-specified intent of study for efficacy data up to W16 was to analyze subjects who received placebo from Day1 & then received tan 5/10 mg at W16,together,in placebo arm.Data has been reported per four arms. ITT population.Data were not collected after W16 in placebo arm,as those who met criteria to continue,switched to active treatment with tan after W16.Pre-specified intent of study was to compare tan vs placebo for data up to & including W16 & comparisons of tan Vs tram for data up to & including W56.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: units on a scale				
least squares mean (standard error)				
Change at Week 2	-3.30 (± 0.25)	-3.84 (± 0.26)	-2.46 (± 0.26)	-2.74 (± 0.21)
Change at Week 4	-4.58 (± 0.29)	-5.32 (± 0.29)	-3.37 (± 0.29)	-3.67 (± 0.25)
Change at Week 8	-5.27 (± 0.31)	-5.85 (± 0.31)	-3.90 (± 0.31)	-4.51 (± 0.27)
Change at Week 16	-6.27 (± 0.35)	-6.69 (± 0.35)	-4.95 (± 0.36)	-5.21 (± 0.30)
Change at Week 24	-5.57 (± 0.41)	-5.92 (± 0.41)	99999 (± 99999)	-4.59 (± 0.35)
Change at Week 32	-5.46 (± 0.42)	-5.71 (± 0.42)	99999 (± 99999)	-4.74 (± 0.35)
Change at Week 40	-5.12 (± 0.43)	-5.24 (± 0.44)	99999 (± 99999)	-4.53 (± 0.36)
Change at Week 48	-4.92 (± 0.43)	-5.14 (± 0.43)	99999 (± 99999)	-4.44 (± 0.37)
Change at Week 56	-4.85 (± 0.45)	-5.23 (± 0.44)	99999 (± 99999)	-4.41 (± 0.36)

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0121
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-0.18
Variability estimate	Standard error of the mean
Dispersion value	0.34

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.05
upper limit	-0.71
Variability estimate	Standard error of the mean
Dispersion value	0.34

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3697
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.89
upper limit	0.33
Variability estimate	Standard error of the mean
Dispersion value	0.31

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0658
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.16
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.3

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0004
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	-0.5
Variability estimate	Standard error of the mean
Dispersion value	0.31

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0013
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.96
upper limit	-0.48
Variability estimate	Standard error of the mean
Dispersion value	0.38

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	-1.21
Variability estimate	Standard error of the mean
Dispersion value	0.38

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3906
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.99
upper limit	0.39
Variability estimate	Standard error of the mean
Dispersion value	0.35

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0082
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	-0.24
Variability estimate	Standard error of the mean
Dispersion value	0.35

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.34
upper limit	-0.97
Variability estimate	Standard error of the mean
Dispersion value	0.35

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0006
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.15
upper limit	-0.58
Variability estimate	Standard error of the mean
Dispersion value	0.4

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.73
upper limit	-1.16
Variability estimate	Standard error of the mean
Dispersion value	0.4

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR

Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1004
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.34
upper limit	0.12
Variability estimate	Standard error of the mean
Dispersion value	0.37

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0385
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.47
upper limit	-0.04
Variability estimate	Standard error of the mean
Dispersion value	0.37

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0003
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.06
upper limit	-0.61
Variability estimate	Standard error of the mean
Dispersion value	0.37

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0035
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.21
upper limit	-0.43
Variability estimate	Standard error of the mean
Dispersion value	0.45

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0002
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.64
upper limit	-0.83
Variability estimate	Standard error of the mean
Dispersion value	0.46

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5412
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.09
upper limit	0.57
Variability estimate	Standard error of the mean
Dispersion value	0.42

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0107
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.87
upper limit	-0.25
Variability estimate	Standard error of the mean
Dispersion value	0.42

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0004
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.29
upper limit	-0.66
Variability estimate	Standard error of the mean
Dispersion value	0.42

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0464
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.94
upper limit	-0.02
Variability estimate	Standard error of the mean
Dispersion value	0.49

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0068
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	-0.37
Variability estimate	Standard error of the mean
Dispersion value	0.49

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR

Statistical analysis description:

Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1485
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0.26
Variability estimate	Standard error of the mean
Dispersion value	0.5

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0507
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.94
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.5

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR

Statistical analysis description:

Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.248
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	0.41
Variability estimate	Standard error of the mean
Dispersion value	0.51

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1605
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.71
upper limit	0.28
Variability estimate	Standard error of the mean
Dispersion value	0.51

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3654
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.55
Variability estimate	Standard error of the mean
Dispersion value	0.52

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1782
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.71
upper limit	0.32
Variability estimate	Standard error of the mean
Dispersion value	0.52

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3981
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.47
upper limit	0.58
Variability estimate	Standard error of the mean
Dispersion value	0.52

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline RMDQ, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1089
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.84
upper limit	0.18
Variability estimate	Standard error of the mean
Dispersion value	0.52

Secondary: Change From Baseline in Roland Morris Disability Questionnaire (RMDQ) Score at Weeks 64 and 80

End point title	Change From Baseline in Roland Morris Disability Questionnaire (RMDQ) Score at Weeks 64 and 80[7]

End point description:

The RMDQ is a self-administered, widely used health status measure index of how well subjects with LBP are able to function with regard to daily activities. It measures pain and function, using 24 items describing limitations to everyday life that can be caused by LBP. The score of the RMDQ is the total number of items checked ranging from 0 (no disability) to 24 (maximum disability), where higher scores indicated greater disability. ITT population included all randomized subjects who received at least one dose of SC study medication (either tanezumab or matching placebo). Here, "n" = subjects evaluable for this end point at specified time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 64 and 80

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 202, 204, 405, 407, 605)	14.64 (± 5.26)	14.98 (± 5.03)	15.02 (± 5.21)	15.06 (± 4.92)
Change at Week 64 (n= 63,141, 149,59,204)	-8.35 (± 6.72)	-8.71 (± 5.78)	-8.72 (± 6.32)	-7.64 (± 5.96)
Change at Week 80 (n= 62,135, 146,59,193)	-8.03 (± 7.00)	-7.27 (± 6.79)	-8.80 (± 6.68)	-7.13 (± 5.99)

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 202, 204, 405, 407, 605)	15.10 (± 5.11)			
Change at Week 64 (n= 63,141, 149,59,204)	-8.87 (± 5.88)			
Change at Week 80 (n= 62,135, 146,59,193)	-8.35 (± 6.01)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Patient's Global Assessment (PGA) of Low Back Pain at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56

End point title	Change from Baseline in Patient's Global Assessment (PGA) of Low Back Pain at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56[8]

End point description:

PGA of LBP assessed by asking question to subjects: "Considering all ways your low back pain affects you, how are you doing today? Subjects responded on 5 point Likert scale ranging 1-5,by IRT. Higher scores indicated worsening of condition. Pre-specified intent of study for efficacy data up to W16 was to analyze subjects who received placebo from Day1 & then received tan 5/10 mg at W16,together,in placebo arm. Data has been reported per four arms. ITT population. Data were not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tan after W16.Pre-specified intent of study was to compare tan vs placebo for data up to & including W16 & comparisons of tan Vs tram for data up to & including W56.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: units on a scale				
least squares mean (standard error)				
Change at Week 2	-0.62 (± 0.04)	-0.67 (± 0.04)	-0.54 (± 0.04)	-0.54 (± 0.03)
Change at Week 4	-0.82 (± 0.04)	-0.86 (± 0.04)	-0.64 (± 0.04)	-0.66 (± 0.04)
Change at Week 8	-0.82 (± 0.05)	-0.89 (± 0.05)	-0.69 (± 0.05)	-0.76 (± 0.04)
Change at Week 16	-0.98 (± 0.05)	-1.02 (± 0.05)	-0.86 (± 0.05)	-0.85 (± 0.04)
Change at Week 24	-0.83 (± 0.06)	-0.82 (± 0.06)	99999 (± 99999)	-0.74 (± 0.05)
Change at Week 32	-0.80 (± 0.06)	-0.79 (± 0.06)	99999 (± 99999)	-0.74 (± 0.05)
Change at Week 40	-0.80 (± 0.06)	-0.75 (± 0.06)	99999 (± 99999)	-0.70 (± 0.05)
Change at Week 48	-0.74 (± 0.07)	-0.72 (± 0.07)	99999 (± 99999)	-0.66 (± 0.06)
Change at Week 56	-0.76 (± 0.06)	-0.74 (± 0.07)	99999 (± 99999)	-0.66 (± 0.06)

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1472
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0135
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	-0.03
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.9149
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0893
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.01
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0044
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	-0.04
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0025
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	-0.06
Variability estimate	Standard error of the mean
Dispersion value	0.06

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0002
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.06

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR

Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8348
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.002
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	-0.06
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0272
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	-0.01
Variability estimate	Standard error of the mean
Dispersion value	0.06

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0009
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.31
upper limit	-0.08
Variability estimate	Standard error of the mean
Dispersion value	0.06

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.168
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2968
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0219
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	-0.02
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0717
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0.01
Variability estimate	Standard error of the mean
Dispersion value	0.07

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0207
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	-0.02
Variability estimate	Standard error of the mean
Dispersion value	0.07

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR

Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8399
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.13
Variability estimate	Standard error of the mean
Dispersion value	0.06

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0299
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	-0.01
Variability estimate	Standard error of the mean
Dispersion value	0.06

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 16:Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.006
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	-0.05
Variability estimate	Standard error of the mean
Dispersion value	0.06

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 24:Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1974
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.07

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.278
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.22
upper limit	0.06
Variability estimate	Standard error of the mean
Dispersion value	0.07

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR

Statistical analysis description:

Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.433
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.07

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4946
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.07

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR

Statistical analysis description:

Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1884
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.08

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.521
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.08

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR

Statistical analysis description:

Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.3329
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	0.08
Variability estimate	Standard error of the mean
Dispersion value	0.08

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 48:Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5173
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.08

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR

Statistical analysis description:

Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2346
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0.06
Variability estimate	Standard error of the mean
Dispersion value	0.08

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline PGA, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3634
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.08

Secondary: Change from Baseline in Patient's Global Assessment (PGA) of Low Back Pain at Week 64

End point title	Change from Baseline in Patient's Global Assessment (PGA) of Low Back Pain at Week 64[9]

End point description:

PGA of LBP was assessed by asking a question to subjects: "Considering all the ways your low back pain affects you, how are you doing today?" Subjects responded on a 5 point Likert scale ranging from 1-5, using IRT, where 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 indicated worsening of condition. ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo). 'Number analyzed' (n) = subjects evaluable for this endpoint at specified time point.

End point type	Secondary

End point timeframe:

Baseline, Week 64

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n= 202, 204, 405, 407, 605)	3.47 (± 0.65)	3.49 (± 0.60)	3.47 (± 0.61)	3.53 (± 0.63)
Change at Week 64(n= 63, 57, 140, 147, 200)	-1.21 (± 1.02)	-1.16 (± 0.86)	-1.03 (± 0.98)	-1.01 (± 0.92)

End point values	Tramadol PR			

Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n= 202, 204, 405, 407, 605) Change at Week 64(n= 63, 57, 140, 147, 200)	3.50 (± 0.63) -1.14 (± 0.88)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Cumulative Percent Change From Baseline in Daily Average Low Back Pain Intensity (ALBPI) Score at Weeks 16, 24 and 56: Mixed Baseline Observation Carried Forward (BOCF)/Last Observation Carried Forward (LOCF)

End point title	Percentage of Subjects With Cumulative Percent Change From Baseline in Daily Average Low Back Pain Intensity (ALBPI) Score at Weeks 16, 24 and 56: Mixed Baseline Observation Carried Forward (BOCF)/Last Observation Carried Forward (LOCF)[10]

End point description:

ALBP:assessed on 11-point NRS captured through an IRT.LBPI score captured once week for W64.Subjects described their average LBP during the past 24 hours on a scale ranging from 0-10 ,where higher scores indicated higher pain. Pre-specified intent of study for efficacy data up to W16 was to analyze, subjects who received placebo from Day 1 and received tan 5/10 mg at week 16 in placebo arm,in pooled manner.Data have been reported per 4 arms.ITT.Data were not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16.Pre-specified intent of was to compare tan Vs placebo for data up to and including week 16 and comparisons of tan Vs tramadol for data up to and including week 56,data is 99999 for placebo arm for week 16 and onwards."N" =subjects evaluable for this endpoint & "n"=subjects evaluable at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 24 and 56

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	406	406	404	605
Units: percentage of subjects				
number (not applicable)				
Change at Week 16: >0% (n =406, 406, 404, 605)	85.3	87.2	80.8	80.8
Change at Week 16: >=10% (n =406, 406, 404, 605)	79.1	82.1	73.6	74.5
Change at Week 16: >=20% (n =406, 406, 404, 605)	72.5	73.2	64.8	64.8
Change at Week 16: >=30% (n =406, 406, 404, 605)	64.6	65.4	55.7	57.9

Change at Week 16: >=40% (n =406, 406, 404, 605)	52.1	56.3	46.8	49.9
Change at Week 16: >=50% (n =406, 406, 404, 605)	43.2	46.2	37.2	42.8
Change at Week 16: >=60% (n =406, 406, 404, 605)	33.4	36.9	29.3	32.2
Change at Week 16: >=70% (n =406, 406, 404, 605)	21.6	25.1	18.5	20.2
Change at Week 16: >=80% (n =406, 406, 404, 605)	13.3	15.7	10.3	13.4
Change at Week 16: >=90% (n =406, 406, 404, 605)	7.4	6.6	5.4	6.3
Change at Week 16: =100% (n =406, 406, 404, 605)	3.9	2.7	2.7	4.1
Change at Week 24: >0% (n =406, 406, 0, 605)	71.9	72.4	99999	66.4
Change at Week 24: >=10% (n =406, 406, 0, 605)	68.5	69.2	99999	63.1
Change at Week 24: >=20% (n =406, 406, 0, 605)	61.8	64.8	99999	58.0
Change at Week 24: >=30% (n =406, 406, 0, 605)	57.6	62.1	99999	53.6
Change at Week 24: >=40% (n =406, 406, 0, 605)	51.5	55.9	99999	47.8
Change at Week 24: >=50% (n =406, 406, 0, 605)	44.1	48.8	99999	41.2
Change at Week 24: >=60% (n =406, 406, 0, 605)	33.7	37.4	99999	32.2
Change at Week 24: >=70% (n =406, 406, 0, 605)	24.4	27.6	99999	23.8
Change at Week 24: >=80% (n =406, 406, 0, 605)	16.5	15.3	99999	14.2
Change at Week 24: >=90% (n =406, 406, 0, 605)	6.2	7.1	99999	6.6
Change at Week 24: =100% (n =406, 406, 0, 605)	3.4	5.2	99999	3.8
Change at Week 56: >0% (n =406, 406, 0, 605)	59.9	61.1	99999	58.2
Change at Week 56: >=10% (n =406, 406, 0, 605)	57.6	58.9	99999	55.7
Change at Week 56: >=20% (n =406, 406, 0, 605)	53.2	55.7	99999	51.2
Change at Week 56: >=30% (n =406, 406, 0, 605)	50.7	53.9	99999	46.8
Change at Week 56: >=40% (n =406, 406, 0, 605)	46.1	50.7	99999	42.1
Change at Week 56: >=50% (n =406, 406, 0, 605)	41.6	45.3	99999	38.7
Change at Week 56: >=60% (n =406, 406, 0, 605)	34.5	36.0	99999	31.1
Change at Week 56: >=70% (n =406, 406, 0, 605)	27.1	27.6	99999	23.3
Change at Week 56: >=80% (n =406, 406, 0, 605)	17.2	19.0	99999	15.5
Change at Week 56: >=90% (n =406, 406, 0, 605)	8.9	10.3	99999	9.3
Change at Week 56: =100% (n =406, 406, 0, 605)	6.7	7.9	99999	6.1

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Average LBPI Reduction of >=30 Percent (%), >=50%, >=70% and >=90% From Baseline at Weeks 2, 4, 8, 12, 16, 24, 32, 40, 48 and 56: Mixed Baseline Observation Carried Forward (BOCF)/Last Observation Carried Forward (LOCF)

End point title	Percentage of Subjects Achieving Average LBPI Reduction of >=30 Percent (%), >=50%, >=70% and >=90% From Baseline at Weeks 2, 4, 8, 12, 16, 24, 32, 40, 48 and 56: Mixed Baseline Observation Carried Forward (BOCF)/Last Observation Carried Forward (LOCF)[11]

End point description:

ALBP: assessed on 11-point NRS captured through IRT.LBPI score was captured once week for week 64.Subjects described their average LBP during the past 24 hours on scale ranging from 0(no pain)-10(worst possible pain),where higher scores indicated higher pain. Pre-specified intent of study for efficacy data up to Week 16 was to analyze, subjects who received placebo from Day 1 and received tanezumab 5/10 mg at week 16 in placebo arm,in pooled manner. Hence data have been reported per four arms. ITT population was analysed. Data were not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16.Pre-specified intent of study was to compare tanezumab Vs placebo for data up to & including week 16 & comparisons of tanezumab Vs tramadol for data up to & including W56. 99999=no data evaluable for placebo arm for week 16 & above.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 12, 16, 24, 32, 40, 48 and 56

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	406	406	404	605
Units: percentage of subjects				
number (not applicable)				
Week 2: At least 30% reduction	31.3	31.8	20.8	28.6
Week 2: At least 50% reduction	13.1	14.8	8.9	11.2
Week 2: At least 70% reduction	5.2	5.7	2.7	3.3
Week 2: At least 90% reduction	1.0	1.7	1.0	0.8
Week 4: At least 30% reduction	47.5	53.2	35.6	42.1
Week 4: At least 50% reduction	26.1	30.8	19.1	23.0
Week 4: At least 70% reduction	12.8	17.7	7.4	9.1
Week 4: At least 90% reduction	2.7	3.7	2.7	2.5
Week 8: At least 30% reduction	56.2	59.4	42.6	51.2
Week 8: At least 50% reduction	35.7	40.1	24.0	31.9
Week 8: At least 70% reduction	15.3	21.7	10.9	14.2
Week 8: At least 90% reduction	4.4	4.4	4.0	3.8
Week 12: At least 30% reduction	61.3	66.5	53.5	56.7
Week 12: At least 50% reduction	41.9	47.3	34.7	38.2
Week 12: At least 70% reduction	19.7	26.4	14.9	19.3
Week 12: At least 90% reduction	7.6	7.9	5.0	6.1
Week 16: At least 30% reduction	64.8	65.5	55.9	57.9
Week 16: At least 50% reduction	43.3	46.3	37.4	42.8

Week 16: At least 70% reduction	21.7	25.1	18.6	20.2
Week 16: At least 90% reduction	7.4	6.7	5.4	6.3
Week 24: At least 30% reduction	57.6	62.1	99999	53.6
Week 24: At least 50% reduction	44.1	48.8	99999	41.2
Week 24: At least 70% reduction	24.4	27.6	99999	23.8
Week 24: At least 90% reduction	6.2	7.1	99999	6.6
Week 32: At least 30% reduction	56.7	57.6	99999	50.6
Week 32: At least 50% reduction	44.6	46.3	99999	39.7
Week 32: At least 70% reduction	27.1	25.6	99999	22.5
Week 32: At least 90% reduction	7.6	9.6	99999	7.3
Week 40: At least 30% reduction	53.0	53.9	99999	49.4
Week 40: At least 50% reduction	43.1	44.8	99999	39.7
Week 40: At least 70% reduction	26.4	28.1	99999	24.1
Week 40: At least 90% reduction	9.6	11.3	99999	7.6
Week 48: At least 30% reduction	52.2	53.0	99999	48.6
Week 48: At least 50% reduction	43.1	44.6	99999	38.7
Week 48: At least 70% reduction	27.1	26.6	99999	23.5
Week 48: At least 90% reduction	9.4	11.1	99999	8.3
Week 56: At least 30% reduction	50.7	53.9	99999	46.8
Week 56: At least 50% reduction	41.6	45.3	99999	38.7
Week 56: At least 70% reduction	27.1	27.6	99999	23.3
Week 56: At least 90% reduction	8.9	10.3	99999	9.3

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 2, >=30%: Odds ratio (OR) and 95% Confidence interval (CI) estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0007
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.26
upper limit	2.39

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 2, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0004
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.29
upper limit	2.44

Statistical analysis title	Pooled Placebo Versus Tramadol PR
Statistical analysis description:	
Week 2, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.	
Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0056
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.13
upper limit	2.05

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR
Statistical analysis description:	
Week 2, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3456
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.14

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.5

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR
Statistical analysis description:	
Week 2, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2771
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.53

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo
Statistical analysis description:	
Week 2, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.	
Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0594
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	2.41

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 2, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0105
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.14
upper limit	2.75

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 2, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.236
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.98

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 2, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR v Placebo
Number of subjects included in analysis	1415
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3746
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.19

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.75

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 2, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0974
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.99

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 2, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0806
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	4.08

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 2, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0407
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	4.47

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 2, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5966
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	2.58

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 2, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1492
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.59

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	2.96

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 2, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.072
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	3.24

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 2, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.9926
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	4

Statistical analysis title	Tanezumab 10 mg Vs Pooled Placebo

Statistical analysis description:

Week 2, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3726
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	6.04

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 2, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7874
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	3.12

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 2, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.795
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.19

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	4.46

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 2, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2065
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	6.68

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 4, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0006
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	2.17

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 4, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.55
upper limit	2.72

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 4, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0387
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	1.71

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 4, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0903
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.24

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.6

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 4, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0006
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.21
upper limit	2.01

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 4, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0166
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	2.09

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 4, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.36
upper limit	2.62

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 4, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1389
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.73

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 4, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2504
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.19

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.59

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 4, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0057
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	1.98

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 4, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0126
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.14
upper limit	2.93

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 4, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.71
upper limit	4.22

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 4, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3485
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.99

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 4, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0642
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.46

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	2.19

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 4, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.48
upper limit	3.14

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 4, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.9819
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	2.31

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 4, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4333
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	3.02

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 4, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.814
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	2

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 4, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.8331
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.09

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	2.4

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 4, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.2682
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	3.12

Statistical analysis title	Tanezumab 5 mg Vs Pooled Placebo

Statistical analysis description:

Week 8, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.31
upper limit	2.29

Statistical analysis title	Tanezumab 10 mg Vs Pooled Placebo

Statistical analysis description:

Week 8, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.49
upper limit	2.61

Statistical analysis title	Pooled Placebo Vs Tramadol PR

Statistical analysis description:

Week 8, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0071
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	1.83

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 8, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.1187
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.22

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.57

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 8, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.011
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	1.79

Statistical analysis title	Tanezumab 5 mg Vs Pooled Placebo

Statistical analysis description:

Week 8, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0003
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	2.39

Statistical analysis title	Tanezumab 10 mg Vs Pooled Placebo

Statistical analysis description:

Week 8, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.57
upper limit	2.87

Statistical analysis title	Pooled Placebo Vs Tramadol PR

Statistical analysis description:

Week 8, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0069
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	1.97

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 8, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.2076
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.19

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.55

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 8, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0072
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	1.86

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 8, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0694
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	2.22

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 8, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.53
upper limit	3.36

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 8, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.121
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	2

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 8, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.6706
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.08

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.54

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 8, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0022
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	2.32

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 8, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7546
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	2.22

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 8, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7347
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	2.24

Statistical analysis title	Pooled Placebo Vs Tramadol PR

Statistical analysis description:

Week 8, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.9029
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.84

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 8, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.6402
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.16

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	2.18

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 8, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.6199
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	2.2

Statistical analysis title	Tanezumab 5 mg Vs Pooled Placebo

Statistical analysis description:

Week 12, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0229
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	1.83

Statistical analysis title	Tanezumab 10 mg Vs Pooled Placebo

Statistical analysis description:

Week 12, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0002
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	2.3

Statistical analysis title	Pooled Placebo Vs Tramadol PR

Statistical analysis description:

Week 12, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.315
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.47

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 12, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.137
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.21

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.57

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 12, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0018
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.17
upper limit	1.97

Statistical analysis title	Tanezumab 5 mg Vs Pooled Placebo

Statistical analysis description:

Week 12, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0342
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.81

Statistical analysis title	Tanezumab 10 mg Vs Pooled Placebo

Statistical analysis description:

Week 12, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0003
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.27
upper limit	2.24

Statistical analysis title	Pooled Placebo Vs Tramadol PR

Statistical analysis description:

Week 12, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.2561
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.51

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 12, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.2358
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.17

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.51

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 12, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.004
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.13
upper limit	1.87

Statistical analysis title	Tanezumab 5 mg Vs Pooled Placebo

Statistical analysis description:

Week 12, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0723
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	2.02

Statistical analysis title	Tanezumab 10 mg Vs Pooled Placebo

Statistical analysis description:

Week 12, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.45
upper limit	2.92

Statistical analysis title	Pooled Placebo Vs Tramadol PR

Statistical analysis description:

Week 12, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0653
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.94

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 12, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.9177
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.4

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR
Statistical analysis description:	
Week 12, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0088
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	2.01

Statistical analysis title	Tanezumab 5 mg Vs Pooled Placebo
Statistical analysis description:	
Week 12, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.	
Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.1197
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	2.83

Statistical analysis title	Tanezumab 10 mg Vs Pooled Placebo

Statistical analysis description:

Week 12, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0913
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	2.92

Statistical analysis title	Pooled Placebo Vs Tramadol PR

Statistical analysis description:

Week 12, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.4317
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	2.19

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 12, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.3498
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.27

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	2.08

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 12, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.2768
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	2.15

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 16, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0101
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.09
upper limit	1.92

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 16, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0054
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.13
upper limit	1.99

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 16, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5493
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.39

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 16, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0269
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.34

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	1.74

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 16, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0144
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	1.8

Statistical analysis title	Tanezumab 5 mg Vs Pooled Placebo

Statistical analysis description:

Week 16, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0846
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.7

Statistical analysis title	Tanezumab 10 mg Vs Pooled Placebo

Statistical analysis description:

Week 16, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0101
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.09
upper limit	1.91

Statistical analysis title	Pooled Placebo Vs Tramadol PR

Statistical analysis description:

Week 16, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0848
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.62

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 16, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.8732
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.32

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 16, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2734
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.48

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 16, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2839
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.7

Statistical analysis title	Tanezumab 10 mg Vs Pooled Placebo

Statistical analysis description:

Week 16, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0238
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	2.07

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 16, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5212
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.53

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 16, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.5954
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.09

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.48

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 16, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0638
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.79

Statistical analysis title	Tanezumab 5 mg Vs Pooled Placebo

Statistical analysis description:

Week 16, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.2661
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	2.44

Statistical analysis title	Tanezumab 10 mg Vs pooled Placebo

Statistical analysis description:

Week 16, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4717
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	2.21

Statistical analysis title	Pooled Placebo Vs Tramadol PR

Statistical analysis description:

Week 16, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tramadol PR v Placebo
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.5798
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	2

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 16, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5027
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.18

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.95

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 16, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.8165
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.77

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 24, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.1996
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.52

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 24, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0074
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	1.83

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 24, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3557
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.45

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 24, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.017
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.36

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	1.75

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR
Statistical analysis description:	
Week 24, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8641
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.38

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR
Statistical analysis description:	
Week 24, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1768
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.62

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 24, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7696
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.55

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 24, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7433
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.78

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 32, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0562
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.28

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.65

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 32, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0274
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	1.71

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 32, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1206
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.58

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 32, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0365
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.69

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 32, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0964
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.71

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 32, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2515
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.19

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.59

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 32, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8122
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.71

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 32, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1848
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	2.13

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 40, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2622
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.49

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 40, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1579
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.54

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 40, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2773
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.15

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.49

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 40, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1032
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.59

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 40, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4418
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.5

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 40, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1608
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.63

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 40, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2628
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	2.02

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 40, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0447
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.55

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	2.39

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 48, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.256
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.49

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 48, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.1741
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.53

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 48, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1647
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.55

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 48, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0619
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.65

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 48, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2025
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.21

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.61

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 48, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2601
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.58

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 48, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5635
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.77

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 48, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1338
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	2.11

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 56, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2137
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.51

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 56, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0256
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.33

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	1.72

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 56, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3531
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.46

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 56, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0358
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.7

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 56, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.184
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.62

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 56, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.125
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.67

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 56, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.8266
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.95

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.48

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 56, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5673
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.72

Secondary: Percentage of Subjects Achieving RMDQ Reduction of >=30%, >=50%, >=70% and >=90% From Baseline at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56: Mixed Baseline Observation Carried Forward (BOCF)/Last Observation Carried Forward (LOCF)

End point title	Percentage of Subjects Achieving RMDQ Reduction of >=30%, >=50%, >=70% and >=90% From Baseline at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56: Mixed Baseline Observation Carried Forward (BOCF)/Last Observation Carried Forward (LOCF)[12]

End point description:

RMDQ: health status measure index of how well subjects with LBP are able to function with regard to daily activities. Measures pain and function using 24 items describing limitations to everyday life. Score of RMDQ is total number of items checked ranging from 0=no disability to 24=maximum disability, higher scores=greater disability. Pre-specified intent of study for efficacy data up to Week 16 was to analyze subjects who received placebo from Day 1 and received tanezumab 5/10 mg at week 16 in placebo arm. Hence, data have been reported per four arms. Comparison of tanezumab Vs placebo for data up to and including week 16 and comparisons of tanezumab Vs tramadol for data up to and including week 56 was pre-specified. Hence, number analyzed is 99999 for placebo arm for week 16 and onwards. ITT population. Data were not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	405	407	406	605
Units: percentage of subjects				
number (not applicable)				
Week 2: At least 30% reduction	32.3	38.3	24.1	29.3
Week 2: At least 50% reduction	20.0	21.4	13.5	16.9
Week 2: At least 70% reduction	10.6	10.3	5.7	6.6
Week 2: At least 90% reduction	4.2	5.4	1.7	2.3
Week 4: At least 30% reduction	46.2	50.4	34.5	39.7
Week 4: At least 50% reduction	30.9	34.2	19.2	25.3
Week 4: At least 70% reduction	17.5	21.1	10.1	10.9
Week 4: At least 90% reduction	7.9	9.6	4.2	3.1
Week 8: At least 30% reduction	52.8	56.8	41.1	48.6
Week 8: At least 50% reduction	36.8	40.8	26.4	33.4
Week 8: At least 70% reduction	23.2	24.8	12.8	16.4
Week 8: At least 90% reduction	12.1	13.8	4.9	6.4
Week 16: At least 30% reduction	58.3	62.2	48.5	52.2
Week 16: At least 50% reduction	46.7	48.2	34.7	38.7
Week 16: At least 70% reduction	32.1	34.6	20.7	22.3
Week 16: At least 90% reduction	17.0	15.5	9.1	8.6
Week 24: At least 30% reduction	50.1	15.5	99999	44.8
Week 24: At least 50% reduction	42.5	45.0	99999	34.0
Week 24: At least 70% reduction	29.4	31.7	99999	20.7
Week 24: At least 90% reduction	16.5	18.4	99999	8.3
Week 32: At least 30% reduction	48.6	49.4	99999	43.0
Week 32: At least 50% reduction	42.0	44.7	99999	35.9
Week 32: At least 70% reduction	29.1	31.9	99999	22.5
Week 32: At least 90% reduction	17.8	17.9	99999	11.6
Week 40: At least 30% reduction	44.9	48.2	99999	41.5
Week 40: At least 50% reduction	38.5	40.8	99999	34.4
Week 40: At least 70% reduction	29.9	29.5	99999	23.3
Week 40: At least 90% reduction	17.3	17.2	99999	11.4
Week 48: At least 30% reduction	43.0	45.2	99999	40.8
Week 48: At least 50% reduction	38.0	37.8	99999	33.2
Week 48: At least 70% reduction	28.4	29.5	99999	22.0
Week 48: At least 90% reduction	16.3	17.7	99999	11.4
Week 56: At least 30% reduction	41.2	46.4	99999	41.5
Week 56: At least 50% reduction	36.5	38.8	99999	32.2
Week 56: At least 70% reduction	27.9	28.5	99999	22.3
Week 56: At least 90% reduction	17.8	18.7	99999	11.7

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Vs Placebo

Statistical analysis description:

Week 2, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo

Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0076
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	2.08

Statistical analysis title	Tanezumab 10 mg Vs Placebo
Statistical analysis description:	
Week 2, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.46
upper limit	2.69

Statistical analysis title	Pooled Placebo Vs Tramadol PR
Statistical analysis description:	
Week 2, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.07
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.31

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.74

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 2, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.2655
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.54

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Week 2, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0022
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.16
upper limit	1.98

Statistical analysis title	Tanezumab 5 mg Vs Placebo

Statistical analysis description:

Week 2, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0125
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	2.35

Statistical analysis title	Tanezumab 10 mg Vs Placebo

Statistical analysis description:

Week 2, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0032
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.21
upper limit	2.54

Statistical analysis title	Pooled Placebo Vs Tramadol PR

Statistical analysis description:

Week 2, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.1528
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.85

Statistical analysis title	Tanezumab 5 mg Vs Tramadol PR

Statistical analysis description:

Week 2, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.1863
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.72

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 2, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0667
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.86

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 2, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0101
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.18
upper limit	3.39

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 2, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0162
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.13
upper limit	3.25

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 2, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5599
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.17

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.99

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 2, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0202
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.09
upper limit	2.68

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 2, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0335
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	2.57

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 2, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0416
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	6.17

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 2, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0075
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.37
upper limit	7.69

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 2, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5374
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.33

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	3.34

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR
Statistical analysis description:	
Week 2, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.082
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	3.89

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR
Statistical analysis description:	
Week 2, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0108
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	4.81

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 4, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0006
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.24
upper limit	2.2

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 4, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.47
upper limit	2.59

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 4, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0963
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.25

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.63

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 4, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0332
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.71

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 4, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0007
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.21
upper limit	2.01

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 4, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.37
upper limit	2.64

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 4, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.6
upper limit	3.05

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 4, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0235
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.43

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	1.95

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 4, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0459
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	1.76

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 4, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.002
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.17
upper limit	2.04

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 4, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0019
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.27
upper limit	2.91

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 4, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.62
upper limit	3.62

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 4, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.6765
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.09

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.65

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 4, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0022
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	2.54

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 4, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.56
upper limit	3.15

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 4, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.027
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	3.63

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 4, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.003
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.35
upper limit	4.38

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 4, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.377
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.74

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	1.44

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 4, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0009
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.49
upper limit	4.79

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 4, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.87
upper limit	5.78

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 8, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0011
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	2.1

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 8, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.41
upper limit	2.47

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 8, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0273
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.33

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	1.72

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 8, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1736
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.54

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 8, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0092
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.09
upper limit	1.81

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 8, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0015
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	2.2

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 8, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.45
upper limit	2.63

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 8, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0164
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.41

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	1.86

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 8, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2857
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.51

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 8, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0149
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	1.8

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 8, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.43
upper limit	3.02

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 8, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.57
upper limit	3.28

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 8, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.118
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.34

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.92

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 8, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0062
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.13
upper limit	2.14

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 8, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0009
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.24
upper limit	2.32

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 8, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0003
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.56
upper limit	4.61

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 8, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.82
upper limit	5.28

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 8, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.312
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.33

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	2.32

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 8, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0019
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	3.14

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 8, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.52
upper limit	3.59

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 16, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0064
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	1.95

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 16, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.32
upper limit	2.31

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 16, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2757
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.15

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.48

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR
Statistical analysis description:	
Week 16, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0575
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.65

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR
Statistical analysis description:	
Week 16, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0015
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.17
upper limit	1.96

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 16, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0007
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	2.16

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 16, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.31
upper limit	2.31

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 16, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2231
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.18

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.53

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 16, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0124
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	1.79

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 16, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0025
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.15
upper limit	1.91

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 16, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0002
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.33
upper limit	2.51

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 16, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.48
upper limit	2.79

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 16, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5701
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.09

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.49

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 16, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0004
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.26
upper limit	2.22

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 16, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	2.46

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 16, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0008
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.35
upper limit	3.17

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 16, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0059
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.19
upper limit	2.83

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 16, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7741
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.94

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.46

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 16, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	3.25

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 16, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0008
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.32
upper limit	2.9

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 24, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.089
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.6

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 24, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0067
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	1.83

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 24, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0072
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.43

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	1.85

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR
Statistical analysis description:	
Week 24, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0004
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	2.06

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR
Statistical analysis description:	
Week 24, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0013
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	2.15

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 24, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.34
upper limit	2.39

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 24, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.51
upper limit	3.3

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 24, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.53

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.72
upper limit	3.71

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR
Statistical analysis description:	
Week 32, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0732
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.62

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR
Statistical analysis description:	
Week 32, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0399
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	1.68

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR

Statistical analysis description:

Week 32, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0536
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	1.67

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 32, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0043
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	1.88

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR

Statistical analysis description:

Week 32, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0143
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.43

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	1.91

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR
Statistical analysis description:	
Week 32, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0007
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	2.16

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR
Statistical analysis description:	
Week 32, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.005
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.17
upper limit	2.38

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 32, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0043
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.18
upper limit	2.4

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR

Statistical analysis description:

Week 40, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2777
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.48

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 40, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0326
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.32

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.7

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR
Statistical analysis description:	
Week 40, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1823
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.55

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR
Statistical analysis description:	
Week 40, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.035
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.71

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR

Statistical analysis description:

Week 40, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0164
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	1.88

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 40, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0257
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	1.84

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 40, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.007
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.64

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.14
upper limit	2.35

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR
Statistical analysis description:	
Week 40, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0085
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.13
upper limit	2.32

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR
Statistical analysis description:	
Week 48, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4925
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.41

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 48, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1534
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.55

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR

Statistical analysis description:

Week 48, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1202
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.6

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 48, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1222
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.23

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.6

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR

Statistical analysis description:

Week 48, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0179
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	1.9

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 48, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0065
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	1.99

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR

Statistical analysis description:

Week 48, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0223
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	2.2

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 48, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0045
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.17
upper limit	2.4

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR

Statistical analysis description:

Week 56, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.9385
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.99

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.28

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR
Statistical analysis description:	
Week 56, >=30%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1093
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.59

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR
Statistical analysis description:	
Week 56, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1631
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.57

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 56, >=50%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0285
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	1.74

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR

Statistical analysis description:

Week 56, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0389
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.81

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 56, >=70%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.024
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.39

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	1.86

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR
Statistical analysis description:	
Week 56, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0063
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.15
upper limit	2.34

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR
Statistical analysis description:	
Week 56, >=90%: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline RMDQ, baseline average LBPI and treatment.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0021
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.22
upper limit	2.47

Secondary: Percentage of Subjects With Cumulative Percent Change From Baseline in Roland Morris Disability Questionnaire (RMDQ) Score at Weeks 16, 24 and 56

End point title	Percentage of Subjects With Cumulative Percent Change From

	Baseline in Roland Morris Disability Questionnaire (RMDQ) Score at Weeks 16, 24 and 56[13]

End point description:

RMDQ is self-administered, widely used health status measure index of how well subjects with LBP are able to function with regard to daily activities. It measures pain and function, using 24 items describing limitations to everyday life that can be caused by LBP. The total score of the RMDQ is the total number of items checked ranging from 0 (no disability) to 24 (maximum disability), where higher scores indicated greater disability..Pre-specified intent of study for efficacy data up to W16 was to analyze subjects who received placebo from Day1 and then received tanezumab 5/10 mg at W16,together,in placebo arm.Data has been reported per four arms. ITT population.Data were not collected after W16 in placebo arm, as those who met criteria to continue,switched to active treatment with tanezumab(tan) after W16.N=subjects evaluable for this endpoint.Intent of study was to compare tan V placebo for data up to & including W16 & comparisons of tan Vs tramadol for data up to & including W56.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 24 and 56

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	405	407	406	605
Units: percentage of subjects				
number (not applicable)				
Change at Week 16: >=0% (n =405, 407, 406, 605)	76.8	83.5	71.2	71.2
Change at Week 16: >=10% (n =405, 407, 406, 605)	72.6	78.4	68.2	66.3
Change at Week 16: >=20% ((n =405, 407, 406, 605)	65.4	70.3	60.6	59.3
Change at Week 16: >=30% (n =405, 407, 406, 605)	58.3	62.2	48.5	52.2
Change at Week 16: >=40% (n =405, 407, 406, 605)	53.1	53.3	42.1	44.3
Change at Week 16: >=50% (n =405, 407, 406, 605)	46.7	48.2	34.7	38.7
Change at Week 16: >=60% (n =405, 407, 406, 605)	38.0	41.0	26.1	30.9
Change at Week 16: >=70% (n =405, 407, 406, 605)	32.1	34.6	20.7	22.3
Change at Week 16: >=80% (n =405, 407, 406, 605)	23.2	26.5	14.8	15.5
Change at Week 16: >=90% (n =405, 407, 406, 605)	17.0	15.5	9.1	9.1
Change at Week 16: =100% (n =405, 407, 406, 605)	13.3	9.3	6.4	4.8
Change at Week 24: >=0% (n =405, 407, 0, 605)	60.5	64.6	99999	57.7
Change at Week 24: >=10% (n =405, 407, 0, 605)	58.3	61.9	99999	55.7
Change at Week 24: >=20% (n =405, 407, 0, 605)	54.6	56.5	99999	51.1
Change at Week 24: >=30% (n =405, 407, 0, 605)	50.1	53.3	99999	44.8
Change at Week 24: >=40% (n =405, 407, 0, 605)	46.7	48.2	99999	39.5

Change at Week 24: >=50% (n =405, 407, 0, 605)	42.5	45.0	99999	34.0
Change at Week 24: >=60% (n =405, 407, 0, 605)	35.8	38.6	99999	26.1
Change at Week 24: >=70% (n =405, 407, 0, 605)	29.4	31.7	99999	20.7
Change at Week 24: >=80% (n =405, 407, 0, 605)	22.2	25.3	99999	14.2
Change at Week 24: >=90% (n =405, 407, 0, 605)	16.5	18.4	99999	8.3
Change at Week 24: =100% (n =405, 407, 0, 605)	11.6	11.5	99999	5.6
Change at Week 56: >0% (n =405, 407, 0, 605)	51.6	56.5	99999	52.6
Change at Week 56: >=10% (n =405, 407, 0, 605)	50.1	54.8	99999	49.9
Change at Week 56: >=20% (n =405, 407, 0, 605)	46.2	50.9	99999	46.0
Change at Week 56: >=30% (n =405, 407, 0, 605)	41.2	46.4	99999	41.5
Change at Week 56: >=40% (n =405, 407, 0, 605)	38.0	42.5	99999	36.2
Change at Week 56: >=50% (n =405, 407, 0, 605)	36.5	38.8	99999	32.2
Change at Week 56: >=60% (n =405, 407, 0, 605)	31.9	33.2	99999	27.1
Change at Week 56: >=70% (n =405, 407, 0, 605)	27.9	28.5	99999	22.3
Change at Week 56: >=80% (n =405, 407, 0, 605)	22.7	24.3	99999	17.2
Change at Week 56: >=90% (n =405, 407, 0, 605)	17.8	18.7	99999	11.7
Change at Week 56: =100% (n =405, 407, 0, 605)	13.8	14.0	99999	7.4

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Worst Pain at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56: Observed Data

End point title	Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Worst Pain at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56: Observed Data[14]

End point description:

BPI-sf: questionnaire developed to assess severity of pain & pain interference on daily functions during 24 hours prior to evaluation. Severity of pain was measured based on questions 1 to 4 of pain at its 'worst', 'least', 'average' and 'right now'. For Worst Pain item of BPI-sf scale(11 point NRS scale; range: 0[no pain] to 10[pain as bad as you can imagine]) .Pre-specified intent for efficacy data up to Week 16 was to analyze, subjects received placebo from Day 1 and received tanezumab(tan)5/10 mg at week16 in placebo arm. Data has been reported per four arms. ITT population. Data were not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16.Intent was to compare tan Vs placebo for data up to & including week 16 & comparisons of tan Vs tramadol for data up to &including week 56.Number analyzed=0 for placebo arm for week 16 & onwards.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: units on a scale				
least squares mean (standard error)				
Change at Week 2	-1.66 (± 0.10)	-1.76 (± 0.10)	-1.17 (± 0.10)	-1.40 (± 0.09)
Change at Week 4	-2.30 (± 0.12)	-2.50 (± 0.12)	-1.73 (± 0.12)	-1.98 (± 0.11)
Change at Week 8	-2.57 (± 0.13)	-2.86 (± 0.13)	-2.11 (± 0.13)	-2.37 (± 0.11)
Change at Week 16	-3.18 (± 0.14)	-3.21 (± 0.14)	-2.67 (± 0.15)	-2.90 (± 0.12)
Change at Week 24	-2.81 (± 0.17)	-3.01 (± 0.17)	0 (± 0)	-2.66 (± 0.14)
Change at Week 32	-2.88 (± 0.17)	-2.95 (± 0.17)	0 (± 0)	-2.63 (± 0.15)
Change at Week 40	-2.70 (± 0.18)	-2.78 (± 0.18)	0 (± 0)	-2.51 (± 0.15)
Change at Week 48	-2.66 (± 0.19)	-2.73 (± 0.18)	0 (± 0)	-2.44 (± 0.15)
Change at Week 56	-2.66 (± 0.19)	-2.74 (± 0.18)	0 (± 0)	-2.45 (± 0.15)

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0003
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	-0.22
Variability estimate	Standard error of the mean
Dispersion value	0.13

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects,

baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.85
upper limit	-0.33
Variability estimate	Standard error of the mean
Dispersion value	0.13

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0615
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	0.01
Variability estimate	Standard error of the mean
Dispersion value	0.12

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0356
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	-0.02
Variability estimate	Standard error of the mean
Dispersion value	0.12

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0032
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	-0.12
Variability estimate	Standard error of the mean
Dispersion value	0.12

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0003
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.88
upper limit	-0.27
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.08
upper limit	-0.46
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR

Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0844
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0258
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	-0.04
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0004
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	-0.23
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0079
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.78
upper limit	-0.12
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.08
upper limit	-0.41
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0977
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.215
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.11
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0016
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	-0.18
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0058
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.88
upper limit	-0.15
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0038
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.91
upper limit	-0.18
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR

Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1707
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.58
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1083
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	0.06
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0734
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.64
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4603
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	0.25
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0799
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.74
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2339
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	0.16
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1199
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	0.08
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.384
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.23
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.68
upper limit	0.14
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2997
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1778
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.71
upper limit	0.13
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3438
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	0.23
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1876
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.71
upper limit	0.14
Variability estimate	Standard error of the mean
Dispersion value	0.22

Secondary: Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Worst Pain at Week 64: Observed Data

End point title	Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Worst Pain at Week 64: Observed Data[15]

End point description:

BPI-sf is a self-administered questionnaire developed to assess the severity of pain and pain interference on daily functions during 24 hours prior to evaluation. Severity of pain was measured based on questions 1 to 4 of pain at its 'worst', 'least', 'average' and 'right now'. For the Worst Pain item of the BPI-sf scale (11 point NRS scale; range: 0 [no pain] to 10 [pain as bad as you can imagine]), subjects were asked to rate their pain by marking an "X" in one of the boxes that best described their pain at its worst, during 24 hours prior to evaluation, higher scores indicated greater pain severity. Question 5 (7-items) assessed level of pain interference on daily activities. ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo).”n”= subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 64

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n=202,204,405,407,605)	7.93 (± 1.18)	7.91 (± 1.09)	7.95 (± 1.11)	7.92 (± 1.19)
Change at Week 64(n=63,57,140,147,200)	-3.90 (± 2.69)	-4.28 (± 2.37)	-4.01 (± 2.68)	-3.61 (± 2.52)

End point values	Tramadol PR			

Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n=202,204,405,407,605)	7.92 (± 1.18)			
Change at Week 64(n=63,57,140,147,200)	-4.23 (± 2.39)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Average Pain at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56: Observed Data

End point title	Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Average Pain at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56: Observed Data[16]

End point description:

BPI-sf: questionnaire developed to assess severity of pain & pain interference on daily functions during 24 hours prior to evaluation. Severity of pain was measured based on questions 1 to 4 of pain at its 'worst', 'least', 'average' and 'right now'. Pre-specified intent of study for efficacy data up to Week 16 was to analyze, subjects who received placebo from Day 1 and received tanezumab 5/10 mg at week 16 in placebo arm, in pooled manner. Hence data have been reported per four arms. ITT population was analyzed. Data were not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16. Pre-specified intent of study was to compare tanezumab Vs placebo for data up to and including week 16 and comparisons of tanezumab Vs tramadol for data up to and including week 56. Hence, number analyzed is 99999 for placebo arm for week 16 and onwards.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: units on a scale				
least squares mean (standard error)				
Change at Week 2	-1.40 (± 0.10)	-1.47 (± 0.10)	-0.93 (± 0.10)	-1.20 (± 0.08)
Change at Week 4	-2.04 (± 0.12)	-2.22 (± 0.12)	-1.52 (± 0.12)	-1.76 (± 0.10)
Change at Week 8	-2.36 (± 0.12)	-2.60 (± 0.12)	-1.90 (± 0.12)	-2.20 (± 0.10)
Change at Week 16	-2.84 (± 0.14)	-2.93 (± 0.14)	-2.47 (± 0.14)	-2.64 (± 0.12)
Change at Week 24	-2.58 (± 0.16)	-2.72 (± 0.16)	99999 (± 99999)	-2.45 (± 0.14)
Change at Week 32	-2.61 (± 0.16)	-2.67 (± 0.16)	99999 (± 99999)	-2.43 (± 0.14)
Change at Week 40	-2.46 (± 0.17)	-2.53 (± 0.17)	99999 (± 99999)	-2.32 (± 0.14)
Change at Week 48	-2.40 (± 0.17)	-2.44 (± 0.17)	99999 (± 99999)	-2.29 (± 0.14)

Change at Week 56	-2.32 (± 0.17)	-2.51 (± 0.17)	99999 (± 99999)	-2.29 (± 0.14)

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0002
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.72
upper limit	-0.22
Variability estimate	Standard error of the mean
Dispersion value	0.13

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	-0.29

Variability estimate	Standard error of the mean
Dispersion value	0.13

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0193
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	-0.04
Variability estimate	Standard error of the mean
Dispersion value	0.12

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0845
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.12

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0212
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	-0.04
Variability estimate	Standard error of the mean
Dispersion value	0.12

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0003
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.81
upper limit	-0.24
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.99
upper limit	-0.41
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf worst pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.079
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random

effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0336
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.55
upper limit	-0.02
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0008
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	-0.19
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0034
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.77
upper limit	-0.15
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.01
upper limit	-0.39
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR

Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0361
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.59
upper limit	-0.02
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2786
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.44
upper limit	0.13
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0058
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.68
upper limit	-0.11
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0365
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.71
upper limit	-0.02
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0092
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	-0.11
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2923
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	0.15
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2231
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.51
upper limit	0.12
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0724
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4776
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.23
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Tanezumab 10 mg Vs Tramadol PR

Statistical analysis description:

Change at Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1482
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.64
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3249
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	0.18
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1997
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	0.13
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4823
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0.25
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2754
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.17
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5861
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.29
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.4346
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	0.23
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8752
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	0.36
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf average pain, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2663
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.17
Variability estimate	Standard error of the mean
Dispersion value	0.2

Secondary: Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Average Pain at Week 64: Observed Data

End point title	Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Average Pain at Week 64: Observed Data[17]

End point description:

BPI-sf is a self-administered questionnaire developed to assess the severity of pain and pain interference on daily functions during 24 hours prior to evaluation. Severity of pain was measured based on questions 1 to 4 of pain at its ‘worst’, ‘least’, ‘average’ and ‘right now’. For the Average Pain item of the BPI-sf scale (11 point NRS scale; range: 0 [no pain] to 10 [pain as bad as you can imagine]), subjects were asked to rate their pain by marking an "X" in one of the boxes that best described their pain during 24 hours prior to evaluation, higher scores indicated greater pain severity. Question 5 (7-items) assessed level of pain interference on daily activities. ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo).”

n”= subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 64

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n=202,204,405,407,605)	6.87 (± 1.20)	7.02 (± 1.15)	7.00 (± 1.18)	6.88 (± 1.21)
Change at Week 64(n=63,57,140,147,200)	-3.75 (± 2.37)	-4.09 (± 1.82)	-3.84 (± 2.23)	-3.39 (± 2.38)

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n=202,204,405,407,605)	6.97 (± 1.21)			
Change at Week 64(n=63,57,140,147,200)	-4.04 (± 2.06)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference Index at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56: Observed Data

End point title	Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference Index at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56: Observed Data[18]

End point description:

BPI-sf: questionnaire assesses severity of pain and PI on daily functions during 24 hours prior to evaluation. Severity of pain was measured based on questions 1 to 4.Question 5(7-items) assessed level of PI on daily activities. PI index was calculated as mean of the seven BPI-sf PI items (question 5a to g),being PI with general activity;mood; walking ability; normal work (outside home and housework);relations with other people; sleep and enjoyment of life. Pre-specified intent for efficacy data up to W16 was to analyze, subjects who received placebo from Day 1 and received tan 5/10 mg at w16 in placebo arm, in pooled manner. Data reported per 4 arms. ITT. Data were not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tan after W16. Pre-specified intent of study was to compare tanVs placebo for data up to and including w16 and comparisons of tanVs tram for data up to and including w56. 99999 signifies no subjects analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: units on a scale				
least squares mean (standard error)				
Change at Week 2	-1.88 (± 0.11)	-1.97 (± 0.11)	-1.40 (± 0.11)	-1.57 (± 0.10)
Change at Week 4	-2.50 (± 0.13)	-2.68 (± 0.13)	-1.90 (± 0.13)	-2.14 (± 0.11)
Change at Week 8	-2.70 (± 0.13)	-2.83 (± 0.13)	-2.26 (± 0.13)	-2.44 (± 0.11)
Change at Week 16	-3.06 (± 0.14)	-3.23 (± 0.14)	-2.65 (± 0.14)	-2.80 (± 0.12)
Change at Week 24	-2.67 (± 0.17)	-2.75 (± 0.16)	99999 (± 99999)	-2.44 (± 0.14)
Change at Week 32	-2.64 (± 0.16)	-2.64 (± 0.16)	99999 (± 99999)	-2.37 (± 0.14)
Change at Week 40	-2.44 (± 0.17)	-2.48 (± 0.17)	99999 (± 99999)	-2.24 (± 0.14)
Change at Week 48	-2.37 (± 0.17)	-2.37 (± 0.17)	99999 (± 99999)	-2.18 (± 0.14)
Change at Week 56	-2.32 (± 0.17)	-2.44 (± 0.17)	99999 (± 99999)	-2.21 (± 0.15)

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0013
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.77
upper limit	-0.19
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.87
upper limit	-0.28
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2272
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.43
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0209
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.58
upper limit	-0.05
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0029
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.67
upper limit	-0.14
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects,

baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0002
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	-0.28
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.46
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR

Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1198
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0.06
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.016
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	-0.07
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0003
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.85
upper limit	-0.25
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0091
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.77
upper limit	-0.11
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0007
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.24
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2264
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	0.11
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0961
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0121
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	-0.08
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.027
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.77
upper limit	-0.05
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0019
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.94
upper limit	-0.21
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR

Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3906
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	0.19
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1209
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.59
upper limit	0.07
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0107
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2396
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	0.15
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1088
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	0.07
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1673
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	0.11
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1751
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	0.12
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3164
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.59
upper limit	0.19
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2253
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	0.15
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3408
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.58
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3391
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.58
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5818
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.28
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference index, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2562
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	0.16
Variability estimate	Standard error of the mean
Dispersion value	0.2

Secondary: Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference Index at Week 64: Observed Data

End point title	Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference Index at Week 64: Observed Data[19]

End point description:

BPI-sf is a self-administered questionnaire developed to assess the severity of pain and pain interference on daily functions during 24 hours prior to evaluation. Severity of pain was measured based on questions 1 to 4. Question 5 (7-items) assessed level of pain interference on daily activities. Pain interference index was calculated as the mean of the seven BPI-sf pain interference items (question 5a to g), being pain interference with general activity; mood; walking ability; normal work (outside home and housework); relations with other people; sleep and enjoyment of life. Responses were given on an 11-point NRS with score ranging from 0 (does not interfere) to 10 (completely interferes), lower scores indicated less pain or pain interference. ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo).”n”= subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 64

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n= 202, 204, 405, 407, 605)	5.85 (± 1.90)	6.20 (± 1.88)	6.28 (± 1.81)	6.16 (± 1.93)
Change at Week 64(n= 63, 57, 140, 147, 200)	-3.87 (± 2.63)	-4.21 (± 1.98)	-4.00 (± 2.44)	-3.60 (± 2.30)

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n= 202, 204, 405, 407, 605)	6.21 (± 1.88)			
Change at Week 64(n= 63, 57, 140, 147, 200)	-3.98 (± 2.10)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference with General Activity at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56: Observed Data

End point title	Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference with General Activity at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56: Observed Data[20]

End point description:

BPI-sf:questionnaire assesses severity of pain and PI on daily functions during 24 hours prior to evaluation.Severity of pain was measured based on questions 1 to 4.Question 5(7-items) assessed level of PI on daily activities.PI index was calculated as mean of the seven BPI-sf PI items (question 5a to g),being PI with general activity;mood; walking ability;normal work (outside home and housework);relations with other people;sleep and enjoyment of life.Responses given on 11-point NRS with score ranging from 0(does not interfere) to10 (completely interferes),lower scores indicated less pain or PI.Pre-specified intent for efficacy data up to W16 was to analyze,subjects who received placebo from Day 1 and received tan 5/10 mg at w16 in placebo arm, in pooled manner.Data reported per 4 arms, intent of study was to compare tanVs placebo for data up to and including w16 and comparisons of tanVs tramadol for data up to and including w56.99999 signifies no subjects analyzed. ITT population.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: units on a scale				
least squares mean (standard error)				
Change at Week 2	-1.84 (± 0.12)	-1.91 (± 0.12)	-1.46 (± 0.12)	-1.53 (± 0.10)
Change at Week 4	-2.45 (± 0.13)	-2.71 (± 0.13)	-1.92 (± 0.13)	-2.14 (± 0.12)
Change at Week 8	-2.68 (± 0.14)	-2.86 (± 0.14)	-2.37 (± 0.14)	-2.54 (± 0.12)
Change at Week 16	-3.20 (± 0.15)	-3.35 (± 0.15)	-2.70 (± 0.15)	-2.89 (± 0.13)
Change at Week 24	-2.78 (± 0.17)	-2.87 (± 0.17)	99999 (± 99999)	-2.87 (± 0.14)
Change at Week 32	-2.74 (± 0.18)	-2.76 (± 0.17)	99999 (± 99999)	-2.52 (± 0.15)

Change at Week 40	-2.54 (± 0.18)	-2.58 (± 0.18)	99999 (± 99999)	-2.40 (± 0.15)
Change at Week 48	-2.47 (± 0.18)	-2.47 (± 0.18)	99999 (± 99999)	-2.33 (± 0.15)
Change at Week 56	-2.44 (± 0.18)	-2.53 (± 0.18)	99999 (± 99999)	-2.39 (± 0.15)

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0137
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	-0.08
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0044
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.45

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	-0.14
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.6194
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.35
upper limit	0.21
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0271
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.31

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.59
upper limit	-0.04
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0085
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0027
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.53

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.87
upper limit	-0.18
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.13
upper limit	-0.44
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1859
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.22

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0573
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	0.01
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0005
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.56

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.88
upper limit	-0.25
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0841
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0074
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.49

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.85
upper limit	-0.13
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.316
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	0.16
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3763
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.15

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	0.18
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0505
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0118
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.49

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.88
upper limit	-0.11
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0012
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.03
upper limit	-0.25
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2966
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.19

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	0.17
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0956
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0117
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.45

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.81
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3732
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	0.21
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1922
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.26

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	0.13
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2986
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	0.19
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2584
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.24

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	0.17
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5195
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	0.29
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3752
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.19

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.22
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5157
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	0.28
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5065
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.14

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	0.28
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8373
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	0.38
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with general activity, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5146
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.14

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	0.28
Variability estimate	Standard error of the mean
Dispersion value	0.22

Secondary: Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference with General Activity at Week 64: Observed Data

End point title	Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference with General Activity at Week 64: Observed Data[21]

End point description:

BPI-sf is a self-administered questionnaire developed to assess the severity of pain and pain interference on daily functions during 24 hours prior to evaluation. Severity of pain was measured based on questions 1 to 4. Question 5 (7-items) assessed level of pain interference on daily activities. Pain interference index was calculated as the mean of the seven BPI-sf pain interference items (question 5a to g), being pain interference with general activity; mood; walking ability; normal work (outside home and housework); relations with other people; sleep and enjoyment of life. Responses were given on an 11-point NRS with score ranging from 0 (does not interfere) to 10 (completely interferes), lower scores indicated less pain or pain interference.ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo).”n”= subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 64

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n=202,204,405,407,605)	6.40 (± 1.81)	6.69 (± 1.75)	6.69 (± 1.70)	6.66 (± 1.82)
Change at Week 64(n=202,204,405,407,605)	-3.87 (± 2.79)	-4.46 (± 2.19)	-4.03 (± 2.74)	-3.72 (± 2.57)

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n=202,204,405,407,605)	6.67 (± 1.75)			

Change at Week 64(n=202,204,405,407,605)	-4.16 (± 2.33)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference with Walking Ability at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56: Observed Data

End point title	Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference with Walking Ability at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56: Observed Data[22]

End point description:

BPI-sf is a self-administered questionnaire developed to assess the severity of pain and pain interference on daily functions during 24 hours prior to evaluation. Severity of pain was measured based on questions 1 to 4. Question 5 (7-items) assessed level of pain interference on daily activities. Pre-specified intent of study for efficacy data up to W16 was to analyze subjects who received placebo from Day1 and then received tanezumab 5/10 mg at W16,together,in placebo arm. Data has been reported per four arms. ITT population.Data were not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16.Pre-specified intent of study was to compare tanezumab Vs placebo for data up to & including W16 & comparisons of tanezumab Vs tramadol for data up to & including W56.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: units on a scale				
least squares mean (standard error)				
Change at Week 2	-1.72 (± 0.12)	-1.89 (± 0.12)	-1.28 (± 0.12)	-1.54 (± 0.10)
Change at Week 4	-2.38 (± 0.13)	-2.55 (± 0.13)	-1.81 (± 0.13)	-2.03 (± 0.12)
Change at Week 8	-2.60 (± 0.13)	-2.73 (± 0.13)	-2.17 (± 0.14)	-2.30 (± 0.11)
Change at Week 16	-2.90 (± 0.15)	-3.15 (± 0.15)	-2.55 (± 0.15)	-2.68 (± 0.13)
Change at Week 24	-2.54 (± 0.17)	-2.73 (± 0.17)	99999 (± 99999)	-2.30 (± 0.14)
Change at Week 32	-2.50 (± 0.17)	-2.59 (± 0.17)	99999 (± 99999)	-2.24 (± 0.14)
Change at Week 40	-2.31 (± 0.17)	-2.46 (± 0.17)	99999 (± 99999)	-2.09 (± 0.15)
Change at Week 48	-2.24 (± 0.17)	-2.34 (± 0.17)	99999 (± 99999)	-2.04 (± 0.14)
Change at Week 56	-2.24 (± 0.17)	-2.45 (± 0.17)	99999 (± 99999)	-2.07 (± 0.14)

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0059
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	-0.13
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0002
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	-0.29

Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0756
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2197
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	0.11
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0208
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	-0.05
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0013
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.91
upper limit	-0.22
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.08
upper limit	-0.39
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1873
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects,

baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0305
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	-0.03
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0013
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.84
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0158
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.78
upper limit	-0.08
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0015
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.91
upper limit	-0.21
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR

Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4173
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	0.19
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0659
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0078
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.74
upper limit	-0.11
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0737
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.72
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0021
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.97
upper limit	-0.22
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4535
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	0.21
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2271
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	0.13
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0086
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.81
upper limit	-0.12
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2243
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	0.15
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0331
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.81
upper limit	-0.03
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1838
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	0.13
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0795
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2847
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	0.18
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0745
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.311
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.59
upper limit	0.19
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1375
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4036
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.58
upper limit	0.23
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with walking ability, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0641
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.21

Secondary: Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference with Walking Ability at Week 64: Observed Data

End point title	Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference with Walking Ability at Week 64: Observed Data[23]

End point description:

BPI-sf is a self-administered questionnaire developed to assess the severity of pain and pain interference on daily functions during 24 hours prior to evaluation. Severity of pain was measured based on questions 1 to 4. Question 5 (7-items) assessed level of pain interference on daily activities. Pain interference index was calculated as the mean of the seven BPI-sf pain interference items (question 5a to g), being pain interference with general activity; mood; walking ability; normal work (outside home and housework); relations with other people; sleep and enjoyment of life. Responses were given on an 11-point NRS with score ranging from 0 (does not interfere) to 10 (completely interferes), lower scores

indicated less pain or pain interference. ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo).”n”= subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 64

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n=202,204,405,407,605)	5.66 (± 2.28)	6.07 (± 2.14)	5.95 (± 2.22)	6.01 (± 2.24)
Change at Week 64(n=63,57,140,147,200)	-3.78 (± 2.91)	-4.14 (± 2.37)	-3.65 (± 2.79)	-3.61 (± 2.65)

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n=202,204,405,407,605)	6.04 (± 2.03)			
Change at Week 64(n=63,57,140,147,200)	-3.78 (± 2.37)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference with Sleep at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56: Observed Data

End point title	Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference with Sleep at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56: Observed Data[24]

End point description:

BPI-sf:questionnaire assesses severity of pain and PI on daily functions during 24 hours prior to evaluation.Severity of pain was measured based on questions 1 to 4.Question 5(7-items) assessed level of PI on daily activities. Pre-specified intent for efficacy data up to W16 was to analyze,subjects who received placebo from Day 1 and received tan 5/10 mg at w16 in placebo arm, in pooled manner.Data reported per 4 arms. ITT population. Data were not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16. Pre-specified intent of study was to compare tanVs placebo for data up to and including w16 and comparisons of tanVs tramadol for data up to and including w56.99999 signifies no subjects analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: units on a scale				
least squares mean (standard error)				
Change at Week 2	-2.09 (± 0.13)	-2.15 (± 0.14)	-1.58 (± 0.14)	-1.80 (± 0.11)
Change at Week 4	-2.79 (± 0.15)	-2.98 (± 0.15)	-2.13 (± 0.15)	-2.34 (± 0.13)
Change at Week 8	-2.94 (± 0.15)	-3.13 (± 0.15)	-2.42 (± 0.15)	-2.70 (± 0.13)
Change at Week 16	-3.38 (± 0.16)	-3.44 (± 0.16)	-2.92 (± 0.16)	-3.00 (± 0.14)
Change at Week 24	-2.89 (± 0.18)	-3.09 (± 0.18)	99999 (± 99999)	-2.59 (± 0.15)
Change at Week 32	-2.88 (± 0.18)	-2.94 (± 0.18)	99999 (± 99999)	-2.54 (± 0.15)
Change at Week 40	-2.64 (± 0.18)	-2.81 (± 0.19)	99999 (± 99999)	-2.41 (± 0.15)
Change at Week 48	-2.61 (± 0.19)	-2.73 (± 0.19)	99999 (± 99999)	-2.34 (± 0.16)
Change at Week 56	-2.57 (± 0.18)	-2.74 (± 0.18)	99999 (± 99999)	-2.37 (± 0.16)

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0037
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.85
upper limit	-0.17
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Pooled Placebo Versus Tanezumab 5 mg

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0013
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.91
upper limit	-0.22
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1712
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0686
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0289
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	-0.04
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Pooled Placebo Versus Tanezumab 5 mg

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects,

baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0003
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.02
upper limit	-0.3
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Pooled Placebo Versus Tanezumab 10 mg

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.22
upper limit	-0.49
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR

Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2056
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.55
upper limit	0.12
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0084
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.78
upper limit	-0.11
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0002
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.98
upper limit	-0.31
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0063
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.15
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0002
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.09
upper limit	-0.34
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1155
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	0.07
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1652
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.59
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0129
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.78
upper limit	-0.09
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Pooled Placebo Versus Tanezumab 5 mg

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0236
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.87
upper limit	-0.06
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Pooled Placebo Versus Tanezumab 10 mg

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0136
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	-0.11
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR

Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.6624
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0468
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	-0.01
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.025
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.81
upper limit	-0.05
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1539
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.72
upper limit	0.11
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0169
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.91
upper limit	-0.09
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1049
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.77
upper limit	0.07
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0599
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.82
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3041
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0737
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.83
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2293
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.71
upper limit	0.17
Variability estimate	Standard error of the mean
Dispersion value	0.23

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0806
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.82
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.368
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	0.23
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with sleep, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0893
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	0.06
Variability estimate	Standard error of the mean
Dispersion value	0.21

Secondary: Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference with Sleep at Week 64: Observed Data

End point title	Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference with Sleep at Week 64: Observed Data[25]

End point description:

BPI-sf is a self-administered questionnaire developed to assess the severity of pain and pain interference on daily functions during 24 hours prior to evaluation. Severity of pain was measured based on questions 1 to 4. Question 5 (7-items) assessed level of pain interference on daily activities. Pain interference index was calculated as the mean of the seven BPI-sf pain interference items (question 5a to g), being pain interference with general activity; mood; walking ability; normal work (outside home and housework); relations with other people; sleep and enjoyment of life. Responses were given on an 11-point NRS with score ranging from 0 (does not interfere) to 10 (completely interferes), lower scores indicated less pain or pain interference.ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo).”n”= subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 64

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n=202,204,405,407,605)	6.45 (± 2.49)	6.73 (± 2.37)	6.88 (± 2.31)	6.67 (± 2.39)
Change at Week 64(n=63,57,140,147,200)	-4.29 (± 3.17)	-4.54 (± 2.80)	-4.19 (± 2.95)	-4.05 (± 2.70)

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n=202,204,405,407,605)	6.82 (± 2.38)			
Change at Week 64(n=63,57,140,147,200)	-4.11 (± 2.78)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference with Normal Work at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56: Observed Data

End point title	Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference with Normal Work at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56: Observed Data[26]

End point description:

BPI-sf: questionnaire assesses severity of pain and PI on daily functions during 24 hours prior to evaluation. Severity of pain was measured based on questions 1 to 4.Question 5(7-items) assessed level of PI on daily activities. Responses given on 11-point NRS with score ranging from 0(does not interfere) to10 (completely interferes),lower scores indicated less pain or PI. Pre-specified intent for efficacy data up to W16 was to analyze, subjects who received placebo from Day 1 and received tan 5/10 mg at w16 in placebo arm, in pooled manner. Data reported per 4 arms. ITT population. Data were not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16.Pre-specified intent of study was to compare tanVs placebo for data up to and including w16 and comparisons of tanVs tramadol for data up to and including w56.99999 signifies no subjects analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: units on a scale				
least squares mean (standard error)				
Change at Week 2	-1.86 (± 0.12)	-2.01 (± 0.12)	-1.30 (± 0.12)	-1.53 (± 0.10)
Change at Week 4	-2.43 (± 0.14)	-2.81 (± 0.14)	-1.92 (± 0.14)	-2.14 (± 0.12)
Change at Week 8	-2.70 (± 0.14)	-2.96 (± 0.14)	-2.32 (± 0.14)	-2.51 (± 0.12)
Change at Week 16	-3.15 (± 0.15)	-3.33 (± 0.16)	-2.64 (± 0.15)	-2.87 (± 0.13)
Change at Week 24	-2.78 (± 0.17)	-2.89 (± 0.17)	99999 (± 99999)	-2.53 (± 0.15)
Change at Week 32	-2.72 (± 0.18)	-2.75 (± 0.18)	99999 (± 99999)	-2.52 (± 0.15)

Change at Week 40	-2.57 (± 0.18)	-2.60 (± 0.18)	99999 (± 99999)	-2.37 (± 0.15)
Change at Week 48	-2.48 (± 0.18)	-2.49 (± 0.18)	99999 (± 99999)	-2.33 (± 0.15)
Change at Week 56	-2.46 (± 0.18)	-2.58 (± 0.18)	99999 (± 99999)	-2.33 (± 0.16)

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0007
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.88
upper limit	-0.24
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Pooled Placebo Versus Tanezumab 10 mg

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.71

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.03
upper limit	-0.38
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1291
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0.07
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.029
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.33

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	-0.03
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 2: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0015
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.77
upper limit	-0.18
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Pooled Placebo Versus Tanezumab 5 mg

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0041
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.52

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.87
upper limit	-0.17
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Pooled Placebo Versus Tanezumab 10 mg

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.25
upper limit	-0.54
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1799
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.22

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.55
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0696
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 4: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.67

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.99
upper limit	-0.35
Variability estimate	Standard error of the mean
Dispersion value	0.16

Statistical analysis title	Pooled Placebo Versus Tanezumab 5 mg

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0387
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.74
upper limit	-0.02
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Pooled Placebo Versus Tanezumab 10 mg

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0005
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.64

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	-0.28
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2768
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.51
upper limit	0.15
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2408
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0.13
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 8: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0064
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.78
upper limit	-0.13
Variability estimate	Standard error of the mean
Dispersion value	0.17

Statistical analysis title	Pooled Placebo Versus Tanezumab 5 mg

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0115
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.51

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.11
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Pooled Placebo Versus Tanezumab 10 mg

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0006
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.08
upper limit	-0.29
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2028
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.23

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.59
upper limit	0.13
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1351
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.64
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 16: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0133
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.46

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.82
upper limit	-0.09
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2157
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	0.15
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 24: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0781
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.36

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3527
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	0.22
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 32: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2994
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.22

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3326
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	0.21
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 40: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2822
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.23

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	0.19
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4932
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	0.28
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 48: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4571
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.16

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.58
upper limit	0.26
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5586
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Change at Week 56: Multiple imputation method was applied for missing data, with imputation dependent on reason for missing data. ANCOVA model for imputed datasets included treatment as fixed effects, baseline BPI-sf pain interference with normal work, and baseline average LBPI as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2664
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.24

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.67
upper limit	0.19
Variability estimate	Standard error of the mean
Dispersion value	0.22

Secondary: Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference with Normal Work at Week 64: Observed Data

End point title	Change From Baseline in Brief Pain Inventory-short Form (BPI-sf) Pain Interference with Normal Work at Week 64: Observed Data[27]

End point description:

BPI-sf is a self-administered questionnaire developed to assess the severity of pain and pain interference on daily functions during 24 hours prior to evaluation. Severity of pain was measured based on questions 1 to 4. Question 5 (7-items) assessed level of pain interference on daily activities. Pain interference index was calculated as the mean of the seven BPI-sf pain interference items (question 5a to g), being pain interference with general activity; mood; walking ability; normal work (outside home and housework); relations with other people; sleep and enjoyment of life. Responses were given on an 11-point NRS with score ranging from 0 (does not interfere) to 10 (completely interferes), lower scores indicated less pain or pain interference.ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo).”n”= subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 64

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n=202,204,405,407,605)	6.31 (± 2.12)	6.62 (± 2.03)	6.65 (± 1.91)	6.65 (± 1.90)
Change at Week 64(n=63,57,140,147,200)	-3.95 (± 2.99)	-4.60 (± 2.46)	-4.15 (± 2.86)	-3.80 (± 2.71)

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n=202,204,405,407,605)	6.56 (± 2.07)			

Change at Week 64(n=63,57,140,147,200)	-4.08 (± 2.39)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Responded for Chronic Low Back Pain Responder Index at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56

End point title	Number of Subjects who Responded for Chronic Low Back Pain Responder Index at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56[28]

End point description:

Chronic LBP responder index analysis:composite endpoint of aLBPI score, PGA of LBP, RMDQ total score. Subjects were successful responders if they had: >=30 percent reduction in mean daily average LBPI from baseline to particular week; decrease of >=30 percent in PGA of low back pain from baseline to particular week or no worsening (increase) in RMDQ total score from baseline to particular week. Pre-specified intent of study for efficacy data up to W16 was to analyze, subjects who received placebo from Day 1 and received tan5/10 mg at W16 in placebo arm, in pooled manner. Data have been reported per four arms. ITT population. Data were not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16. Pre-specified intent of study was to compare tan Vs placebo for data up to and including W16 & comparisons of tan Vs tram for data up to and including W56.Number analyzed is 99999 for placebo arm for W16 and onwards.

End point type	Secondary

End point timeframe:

Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Tramadol PR	Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	404	406	605	404
Units: count of subjects				
Week 2	62	76	74	32
Week 4	115	130	134	67
Week 8	131	151	178	86
Week 16	168	179	211	136
Week 24	166	158	207	99999
Week 32	158	160	204	99999
Week 40	158	149	202	99999
Week 48	148	140	197	99999
Week 56	140	144	192	99999

Statistical analyses

Statistical analysis title	Pooled Placebo Versus Tanezumab 5 mg
Statistical analysis description:	
Week 2: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.	
Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.36
upper limit	3.36

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo
Statistical analysis description:	
Week 2: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.	
Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.73
upper limit	4.16

Statistical analysis title	Pooled Placebo Versus Tramadol PR
Statistical analysis description:	
Week 2: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.	
Comparison groups	Placebo v Tramadol PR

Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.03
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	2.51

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 4: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.44
upper limit	2.86

Statistical analysis title	Pooled Placebo Versus Tanezumab 10 mg

Statistical analysis description:

Week 4: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.37

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.69
upper limit	3.32

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 4: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.029
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	1.99

Statistical analysis title	Pooled Placebo Versus Tanezumab 5 mg

Statistical analysis description:

Week 8: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0003
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.31
upper limit	2.47

Statistical analysis title	Pooled Placebo Versus Tanezumab 10 mg

Statistical analysis description:

Week 8: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.62
upper limit	3.03

Statistical analysis title	Placebo Versus Tramadol PR

Statistical analysis description:

Week 8: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0033
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.16
upper limit	2.1

Statistical analysis title	Pooled Placebo Versus Tanezumab 5 mg

Statistical analysis description:

Week 16: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	808
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0179
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.41

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	1.88

Statistical analysis title	Pooled Placebo Versus Tanezumab 5 mg

Statistical analysis description:

Week 16: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.0021
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.18
upper limit	2.08

Statistical analysis title	Placebo Versus Tramadol PR

Statistical analysis description:

Week 16: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.6629
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.38

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 24: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0251
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	1.75

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 24: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1278
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.59

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 32: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0749
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.27

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.65

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 32: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0633
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.66

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 40: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0626
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.67

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 40: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2727
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.51

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 48: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1749
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.57

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 48: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5239
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.09

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.42

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 56: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1009
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3336
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.49

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 56: OR and 95% CI estimated from logistic regression model. Logistic regression model included treatment as fixed effect and baseline average LBPI, baseline PGA, and baseline RMDQ as covariates.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2163
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.54

Secondary: Percentage of Subjects Achieving Improvement of >=2 Points in Patient's Global Assessment (PGA) of Low Back Pain From Baseline at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56:Mixed Baseline Observation Carried Forward (BOCF)/ Last

Observation CF (LOCF)	
End point title	Percentage of Subjects Achieving Improvement of >=2 Points in Patient's Global Assessment (PGA) of Low Back Pain From Baseline at Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56:Mixed Baseline Observation Carried Forward (BOCF)/ Last Observation CF (LOCF)[29]

End point description:

PGA of LBP assessed by asking a question to subjects: "Considering all the ways your low back pain affects you, how are you doing today?" Subjects responded on a 5 point Likert scale ranging from 1-5, using IRT, Higher scores indicated worsening of condition. Missing data was imputed using mixed BOCF/LOCF. Pre-specified intent for efficacy data up to W16 was to analyze, subjects who received placebo from Day 1 and received tan 5/10 mg at w16 in placebo arm, in pooled manner. Data reported per 4 arms. ITT population.Data were not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tan after W16. Intent of study was to compare tan Vs placebo for data up to and including w16 and comparisons of tan Vs tramadol for data up to and including w56.99999 signifies no subjects analyzed. ITT population. Here,"N"=subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 16, 24, 32, 40, 48 and 56

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	405	407	406	605
Units: percentage of subjects				
number (not applicable)				
Week 2	11.1	14.7	9.4	10.1
Week 4	20.5	21.4	13.8	15.0
Week 8	20.2	24.1	15.3	18.8
Week 16	27.4	30.0	22.7	22.5
Week 24	25.9	25.1	99999	21.5
Week 32	25.2	23.1	99999	20.7
Week 40	25.9	25.1	99999	20.7
Week 48	23.2	22.4	99999	20.5
Week 56	24.2	21.1	99999	20.5

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 2: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 5 mg v Placebo

Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.326
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	2.08

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo
Statistical analysis description:	
Week 2: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.	
Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0445
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	2.56

Statistical analysis title	Pooled Placebo Versus Tramadol PR
Statistical analysis description:	
Week 2: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.	
Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.9263
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.61

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 2: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3194
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.94

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 2: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0308
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	2.38

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 4: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0048
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	2.69

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 4: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0114
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	2.51

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 4: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7857
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.56

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 4: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0041
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.18
upper limit	2.44

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 4: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0109
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	2.28

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 8: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0363
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	2.27

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 8: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.004
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	2.59

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 8: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1992
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.27

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.84

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 8: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3084
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.7

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 8: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0586
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.94

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 16: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	811
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.063
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.97

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 16: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0347
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	2.04

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 16: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.79
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.96

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.33

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 16: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0207
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	2

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 16: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0093
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	2.07

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 24: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.04
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.91

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 24: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2478
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.65

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 32: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0304
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.24

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	1.96

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 32: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4763
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.56

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 40: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0178
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	2.01

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 40: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5223
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.53

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 48: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1708
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.72

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 48: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.6022
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.09

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.5

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 56: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1010
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0846
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.81

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 56: OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline PGA of low back pain, baseline average LBPI, and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.9626
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.39

Secondary: European Quality of Life- 5 Dimension-5 Levels (EQ-5D-5L) Dimensions Score

End point title	European Quality of Life- 5 Dimension-5 Levels (EQ-5D-5L)

	Dimensions Score[30]

End point description:

EQ-5D-5L:standardized subjects completed questionnaire that measures health-related quality of life (QOL) and translates that score into an index value or utility score.EQ-5D-5L consists of two components: a health state profile and an optional visual analogue scale (VAS).EQ-5D health state profile is comprised of 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Individual dimension scores ranged from 1.0 (least impairment of health state) to 5.0 (most impairment of health state).Each dimension has 5 levels:1=no problems, 2=slight problems, 3=moderate problems, 4=severe problems, and 5=extreme problems. Health utility score for a subject with no problems in all 5 items is 1 for all countries (except for Zimbabwe where it is 0.9), and is reduced where a subject reports greater levels of problems across the five dimensions. ITT population was analyzed and "n"= subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 8, 16, 24, 40 and 56

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline:Mobility(n=202,204,405,407,605)	2.5 (± 0.84)	2.6 (± 0.88)	2.5 (± 0.83)	2.6 (± 0.82)
Baseline:Self-care(n=202,204,405,407,605)	2.0 (± 0.95)	2.1 (± 0.97)	2.0 (± 0.95)	2.0 (± 0.92)
Baseline:Usual activities(n=202,204,405,407,605)	2.8 (± 0.90)	2.8 (± 0.83)	2.8 (± 0.82)	2.8 (± 0.80)
Baseline:Pain/Discomfort(n=202,204,405,407,605)	3.3 (± 0.73)	3.4 (± 0.71)	3.4 (± 0.68)	3.3 (± 0.69)
Baseline:Anxiety/Depression(n=202,204,405,407,605)	1.8 (± 0.99)	1.9 (± 1.03)	1.9 (± 1.01)	1.9 (± 0.98)
Week 8: Mobility(n=183,184,374,375,557)	1.9 (± 0.78)	2.0 (± 0.90)	1.8 (± 0.85)	1.8 (± 0.81)
Week 8: Selfcare(n=183,184,374,375,557)	1.5 (± 0.71)	1.7 (± 0.79)	1.4 (± 0.66)	1.4 (± 0.65)
Week8:Usual activities(n=183,184,374,375,557)	2.2 (± 0.81)	2.2 (± 0.89)	2.0 (± 0.85)	2.0 (± 0.82)
Week8:Pain/Discomfort(n=183,184,374,375,557)	2.7 (± 0.82)	2.6 (± 0.84)	2.5 (± 0.80)	2.4 (± 0.80)
Week8:Anxiety/Depression(n=183,184,374,375,557)	1.5 (± 0.81)	1.6 (± 0.92)	1.5 (± 0.83)	1.5 (± 0.78)
Week16: Mobility(n=161,163,333,338,452)	1.7 (± 0.82)	1.8 (± 0.85)	1.7 (± 0.78)	1.6 (± 0.75)
Week16:Self-care(n=161,163,333,338,452)	1.4 (± 0.64)	1.5 (± 0.72)	1.3 (± 0.62)	1.3 (± 0.61)
Week16: Usual activities(n=161,163,333,338,452)	1.9 (± 0.81)	2.0 (± 0.85)	1.8 (± 0.84)	1.8 (± 0.80)
Week16: Pain/Discomfort(n=161,163,333,338,45	2.3 (± 0.90)	2.4 (± 0.86)	2.2 (± 0.83)	2.2 (± 0.75)
Week16: Anxiety/Depression(n=161,163,333,338	1.4 (± 0.68)	1.5 (± 0.82)	1.5 (± 0.83)	1.4 (± 0.77)
Week24: Mobility(n=86, 88,222,227,285)	1.5 (± 0.63)	1.6 (± 0.79)	1.6 (± 0.75)	1.5 (± 0.66)

Week24: Selfcare(n=86, 88,222,227,285)	1.3 (± 0.47)	1.4 (± 0.75)	1.3 (± 0.58)	1.2 (± 0.51)
Week24: Usual activities(n=86, 88,222,227,285)	1.6 (± 0.68)	1.7 (± 0.71)	1.6 (± 0.71)	1.7 (± 0.67)
Week24: Pain/Discomfort(n=86, 88,222,227,285)	2.0 (± 0.64)	1.9 (± 0.70)	2.1 (± 0.76)	2.0 (± 0.74)
Week24: Anxiety/Depression(n=86,88,222,227,2	1.2 (± 0.44)	1.3 (± 0.64)	1.4 (± 0.73)	1.3 (± 0.65)
Week40: Mobility(n=70, 73,162,174,225)	1.5 (± 0.76)	1.5 (± 0.62)	1.5 (± 0.75)	1.5 (± 0.70)
Week40: Selfcare(n=70, 73,162,174,225)	1.2 (± 0.62)	1.3 (± 0.53)	1.2 (± 0.46)	1.2 (± 0.45)
Week 40:Usualactivities(n=70, 73,162,174,225)	1.6 (± 0.69)	1.6 (± 0.73)	1.6 (± 0.72)	1.7 (± 0.68)
Week 40:Pain/Discomfort(n=70,73,162,174,2	1.9 (± 0.62)	1.9 (± 0.64)	2.0 (± 0.73)	1.9 (± 0.75)
Week40: Anxiety/Depression(n=70,73,162,174,2	1.2 (± 0.49)	1.3 (± 0.60)	1.3 (± 0.64)	1.3 (± 0.68)
Week56: Mobility(n=62, 62,134,154,197)	1.4 (± 0.61)	1.5 (± 0.72)	1.5 (± 0.69)	1.4 (± 0.67)
Week 56: Self-care(n=62,62,134,154,197)	1.1 (± 0.44)	1.3 (± 0.52)	1.2 (± 0.55)	1.2 (± 0.43)
Week 56:Usualactivities(n=62, 62,134,154,197)	1.6 (± 0.82)	1.6 (± 0.69)	1.6 (± 0.78)	1.6 (± 0.73)
Week 56:Pain/Discomfort(n=62,62,134,154,1	2.0 (± 0.77)	1.9 (± 0.66)	2.0 (± 0.72)	1.9 (± 0.72)
Week 56:Anxiety/Depression(n=62,62,134,15	1.3 (± 0.54)	1.3 (± 0.55)	1.4 (± 0.77)	1.3 (± 0.70)

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline:Mobility(n=202,204,405,407,605)	2.6 (± 0.86)			
Baseline:Self-care(n=202,204,405,407,605)	2.0 (± 0.95)			
Baseline:Usual activities(n=202,204,405,407,605)	2.8 (± 0.84)			
Baseline:Pain/Discomfort(n=202,204,405,407,605)	3.3 (± 0.70)			
Baseline:Anxiety/Depression(n=202,204,405,407,605)	1.9 (± 1.00)			
Week 8: Mobility(n=183,184,374,375,557)	1.9 (± 0.87)			
Week 8: Selfcare(n=183,184,374,375,557)	1.5 (± 0.73)			
Week8:Usual activities(n=183,184,374,375,557)	2.1 (± 0.91)			
Week8:Pain/Discomfort(n=183,184,374,375,557)	2.5 (± 0.79)			
Week8:Anxiety/Depression(n=183,184,374,375,557)	1.6 (± 0.84)			
Week16: Mobility(n=161,163,333,338,452)	1.8 (± 0.79)			

Week16:Self-care(n=161,163,333,338,452)	1.5 (± 0.69)			
Week16: Usual activities(n=161,163,333,338,452)	1.9 (± 0.82)			
Week16: Pain/Discomfort(n=161,163,333,338,45	2.3 (± 0.76)			
Week16: Anxiety/Depression(n=161,163,333,338	1.5 (± 0.79)			
Week24: Mobility(n=86, 88,222,227,285)	1.7 (± 0.75)			
Week24: Selfcare(n=86, 88,222,227,285)	1.3 (± 0.59)			
Week24: Usual activities(n=86, 88,222,227,285)	1.7 (± 0.72)			
Week24: Pain/Discomfort(n=86, 88,222,227,285)	2.1 (± 0.75)			
Week24: Anxiety/Depression(n=86,88,222,227,2	1.3 (± 0.66)			
Week40: Mobility(n=70, 73,162,174,225)	1.6 (± 0.73)			
Week40: Selfcare(n=70, 73,162,174,225)	1.3 (± 0.62)			
Week 40:Usualactivities(n=70, 73,162,174,225)	1.7 (± 0.76)			
Week 40:Pain/Discomfort(n=70,73,162,174,2	2.0 (± 0.72)			
Week40: Anxiety/Depression(n=70,73,162,174,2	1.4 (± 0.63)			
Week56: Mobility(n=62, 62,134,154,197)	1.6 (± 0.83)			
Week 56: Self-care(n=62,62,134,154,197)	1.4 (± 0.66)			
Week 56:Usualactivities(n=62, 62,134,154,197)	1.7 (± 0.82)			
Week 56:Pain/Discomfort(n=62,62,134,154,1	2.0 (± 0.74)			
Week 56:Anxiety/Depression(n=62,62,134,15	1.3 (± 0.63)			

Statistical analyses

No statistical analyses for this end point

Secondary: European Quality of Life- 5 Dimension-5 Levels (EQ-5D-5L) Overall Health Utility Score/ Index Value

End point title	European Quality of Life- 5 Dimension-5 Levels (EQ-5D-5L) Overall Health Utility Score/ Index Value[31]

End point description:

EQ-5D-5L: standardized subject completed questionnaire that measures health-related QOL and translates that score into an index value or utility score.EQ-5D-5L consists of 2 components: a health state profile and an optional VAS.EQ-5D health state profile comprises of 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Individual dimension scores ranged from 1.0 to 5.0. Each dimension has 5 levels: 1=no problems, 2=slight problems, 3=moderate problems, 4=severe problems, and 5=extreme problems. Responses from five domains were used to calculate a single utility index (Overall health utility score) where values are <= 1.Overall health utility score for a subject with no problems in all 5 items is 1 for all countries (except for Zimbabwe where it is 0.9), and reduced where subject reports greater levels of problems across five dimensions. ITT population and "n"= subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 8, 16, 24, 40 and 56

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n=202,204,405,407,605)	0.62 (± 0.16)	0.61 (± 0.15)	0.61 (± 0.16)	0.62 (± 0.16)
Week 8(n=183,184,374,375,557)	0.74 (± 0.13)	0.71 (± 0.14)	0.75 (± 0.13)	0.76 (± 0.14)
Week 16(n=161,163,333,338,452)	0.77 (± 0.14)	0.75 (± 0.14)	0.78 (± 0.14)	0.79 (± 0.13)
Week 24(n=86, 88,222,227,285)	0.82 (± 0.10)	0.81 (± 0.13)	0.80 (± 0.13)	0.82 (± 0.12)
Week 40(n=70, 73, 162,174,225)	0.83 (± 0.11)	0.82 (± 0.12)	0.82 (± 0.12)	0.83 (± 0.12)
Week 56(n=62, 62,134,154,197)	0.85 (± 0.11)	0.82 (± 0.13)	0.82 (± 0.14)	0.84 (± 0.12)

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline(n=202,204,405,407,605)	0.61 (± 0.16)			
Week 8(n=183,184,374,375,557)	0.74 (± 0.14)			
Week 16(n=161,163,333,338,452)	0.77 (± 0.13)			
Week 24(n=86, 88,222,227,285)	0.80 (± 0.12)			
Week 40(n=70, 73, 162,174,225)	0.80 (± 0.14)			
Week 56(n=62, 62,134,154,197)	0.81 (± 0.14)			

Statistical analyses

No statistical analyses for this end point

Secondary: Work Productivity and Activity Impairment Questionnaire for Low Back Pain (WPAI:LBP) Scores at Baseline: Observed Data

End point title	Work Productivity and Activity Impairment Questionnaire for Low Back Pain (WPAI:LBP) Scores at Baseline: Observed Data[32]

End point description:

WPAI: LBP is 6-question subject rated questionnaire that measures the effect of subject's chronic low back pain (CLBP) on general health and symptom severity on work productivity and regular activities. It yields 4 sub-scores: work time missed due to pain (absenteeism), impairment while working (presenteeism), overall work impairment (work productivity) and activity impairment (daily activity

impairment). These sub-scores are expressed as an impairment percentage (range from 0 to 100), with higher numbers indicating greater impairment and less productivity.Pre-specified intent for efficacy data up to W16 was to analyze, subjects who received placebo from Day 1 and received tan 5/10 mg at w16 in placebo arm, in pooled manner. Data reported per 4 arms. ITT population was analyzed and "n"= subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Baseline

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: units on a scale				
arithmetic mean (standard deviation)				
Percent Work TimeMissed(n=236,236,232,316)	11.1 (± 21.03)	10.8 (± 19.89)	8.2 (± 17.43)	10.7 (± 20.12)
PercentImpairment WhileWorking(n=230,232,229,313)	60.8 (± 19.68)	60.6 (± 20.56)	57.9 (± 21.25)	61.2 (± 19.83)
Percent Overall WorkImpairment(n=230,232,229, 313)	63.2 (± 20.34)	63.1 (± 21.69)	60.2 (± 22.11)	63.6 (± 20.93)
Percent Activity Impairment(n=405,407,406,605)	66.6 (± 17.57)	65.1 (± 18.33)	65.7 (± 18.13)	65.4 (± 18.31)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Work Productivity and Activity Impairment Questionnaire for Low Back Pain (WPAI:LBP) Scores at Weeks 16, 56 and 64

End point title	Change from Baseline in Work Productivity and Activity Impairment Questionnaire for Low Back Pain (WPAI:LBP) Scores at Weeks 16, 56 and 64[33]

End point description:

WPAI: LBP:6-question subject rated questionnaire that measures effect of subject's chronic LBP on general health and symptom severity on work productivity and regular activities.4 sub-scores: work time missed due to pain, impairment while working, overall work impairment and activity impairment. Pre-specified intent of study for efficacy data up to W16 was to analyze subjects who received placebo from Day1 and then received tan 5/10 mg at W16, together, in placebo arm. Data has been reported per four arms. ITT population. Data were not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16. Pre-specified intent of study was to compare tan Vs placebo for data up to and including w16 and comparisons of tanezumab Vs tramadol for data up to & including W56. "n"= subjects evaluable for this endpoint for specified rows.'99999' = no subjects were evaluable, hence mean and SD not applicable. Change at Week: CAW.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 56 and 64

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: units on a scale				
least squares mean (standard error)				
Change at Week 16:Absenteeism (n=179,174,171,208)	-5.07 (± 1.15)	-5.89 (± 1.16)	-5.82 (± 1.18)	-5.68 (± 1.07)
CAW16:%Impairment While Working(n=173,170,166,204)	-29.49 (± 1.71)	-30.22 (± 1.72)	-25.46 (± 1.75)	-27.11 (± 1.58)
CAW16:%Overall Work Impairment(n=173,170,166,204)	-30.49 (± 1.75)	-31.95 (± 1.77)	-26.54 (± 1.80)	-28.29 (± 1.62)
CAW16:%Activity Impairment(n=337,343,329,457)	-32.25 (± 1.38)	-32.25 (± 1.38)	-28.07 (± 1.39)	-30.83 (± 1.23)
CAW56:%Work Time Missed (n=77,77,0,87)	-8.06 (± 1.11)	-7.48 (± 1.11)	99999 (± 99999)	-7.19 (± 1.05)
CAW56:%Impairment While Working(n=76,76,0,87)	-39.38 (± 2.03)	-41.32 (± 2.02)	99999 (± 99999)	-38.51 (± 1.89)
CAW56:%Overall Work Impairment(n=76,76,0,87)	-41.18 (± 2.18)	-42.63 (± 2.18)	99999 (± 99999)	-39.25 (± 2.04)
CAW56:%Activity Impairment(n=134,154,0,197)	-43.53 (± 1.75)	-44.16 (± 1.63)	99999 (± 99999)	-43.00 (± 1.47)

Statistical analyses

Statistical analysis title	Pooled Placebo versus Tanezumab 5 mg

Statistical analysis description:

Change at Week 16: Percent Work Time Missed: ANCOVA model included treatment as fixed effects, baseline WPAI score and baseline diary average pain as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.6508
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.49
upper limit	3.98
Variability estimate	Standard error of the mean
Dispersion value	1.64

Statistical analysis title	Pooled Placebo versus Tanezumab 10 mg

Statistical analysis description:

Change at Week 16: Percent Work Time Missed: ANCOVA model included treatment as fixed effects, baseline WPAI score and baseline diary average pain as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.9629
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.33
upper limit	3.18
Variability estimate	Standard error of the mean
Dispersion value	1.66

Statistical analysis title	Pooled Placebo versus Tramadol PR

Statistical analysis description:

Change at Week 16: Percent Work Time Missed: ANCOVA model included treatment as fixed effects, baseline WPAI score and baseline diary average pain as covariates, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.9295
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.99
upper limit	3.27
Variability estimate	Standard error of the mean
Dispersion value	1.59

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR

Statistical analysis description:

Change at Week 16: Percent Work Time Missed: ANCOVA model included treatment as fixed effects, baseline WPAI score and baseline diary average pain as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7007
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.48
upper limit	3.69
Variability estimate	Standard error of the mean
Dispersion value	1.57

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 16: Percent Work Time Missed: ANCOVA model included treatment as fixed effects, baseline WPAI score and baseline diary average pain as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8902
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.32
upper limit	2.88
Variability estimate	Standard error of the mean
Dispersion value	1.58

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR

Statistical analysis description:

Change at Week 56: Percent Work Time Missed: ANCOVA model included treatment as fixed effects, baseline WPAI score and baseline diary average pain as covariates, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5698
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.87

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.89
upper limit	2.15
Variability estimate	Standard error of the mean
Dispersion value	1.53

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Change at Week 56: Percent Work Time Missed: ANCOVA model included treatment as fixed effects, baseline WPAI score and baseline diary average pain as covariates, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8464
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.32
upper limit	2.72
Variability estimate	Standard error of the mean
Dispersion value	1.53

Secondary: Number of Subjects Who Withdrew Due to Lack of Efficacy

End point title	Number of Subjects Who Withdrew Due to Lack of Efficacy[34]

End point description:

Number of subjects who withdrew from treatment due to lack of efficacy have been reported here. ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo).

End point type	Secondary

End point timeframe:

Baseline up to Week 56

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: subjects	25	41	41	46

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: subjects	65			

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR
Statistical analysis description:	
OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7366
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.41

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR
Statistical analysis description:	
OR and 95% CI estimated from logistic regression model. Logistic regression model included baseline average LBPI and treatment.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.771
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.58

Secondary: Time to Discontinuation Due to Lack of Efficacy

End point title	Time to Discontinuation Due to Lack of Efficacy[35]

End point description:

Time to discontinuation due to lack of efficacy was defined as the time interval from the date of first study drug administration up to the date of discontinuation of subject from treatment due to lack of efficacy. ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo). Here, "N" signifies subjects who discontinued from the study due to lack of efficacy. Here, 100 signifies that due to the Kaplan-Meier estimate not reaching the level for discontinuation due to insufficient clinical response, lack of efficacy, median could not be calculated.

End point type	Secondary

End point timeframe:

Baseline up to Week 56

Notes:

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: days				
median (full range (min-max))	100 (14 to 123)	100 (8 to 122)	100 (14 to 252)	100 (2 to 175)

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: days				
median (full range (min-max))	100 (2 to 314)			

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Missing data for the selected percentile(s) was due to the Kaplan-Meier estimate not reaching the level for discontinuation due to lack of efficacy.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4724
Method	Logrank

Statistical analysis title	Tanezumab 10 mg Versus Tramadol

Statistical analysis description:

Missing data for the selected percentile(s) was due to the Kaplan-Meier estimate not reaching the level for discontinuation due to lack of efficacy.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7142
Method	Logrank

Secondary: Number of Subjects Who Took Rescue Medication During Weeks 2, 4, 8, 12, 16, 24, 32, 40, 48, 56 and 64

End point title	Number of Subjects Who Took Rescue Medication During Weeks 2, 4, 8, 12, 16, 24, 32, 40, 48, 56 and 64[36]

End point description:

In case of inadequate pain relief, acetaminophen/paracetamol caplets, tablets, or capsules up to 3000 mg per day up to 3 days in a week could be taken as rescue medication between day 1 and week 56. Number of subjects with any use of rescue medication during the particular study week were summarized. For analyses after week 16 where multiple imputation was used, data was reported per 3 arms. This is because subjects who received placebo from Day 1 and received tanezumab 5/10 mg at week 16, received placebo for the first 16 weeks, and their data before week 16 were not be imputed into analyses after week 16. ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo). Here," Number of Subjects Analyzed (N)"=subjects evaluable for this end point and "number analysed (n)" subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Weeks 2, 4, 8, 12, 16, 24, 32, 40, 48, 56 and 64

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Tramadol PR	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	407	407	604	
Units: subjects				
Week 2(n=406,406,402)	226	208	318	
Week 4(n=407,407,604)	205	175	285	
Week (n=407,407,604)	176	158	250	
Week 12(n=407,407,604)	150	147	216	
Week 16(n=407,407,604)	134	125	193	

Week 24(n=407,407,604)	145	150	211	
Week 32(n=407,407,604)	146	152	210	
Week 40(n=407,407,604)	145	144	209	
Week 48(n=407,407,604)	141	144	210	
Week 56(n=407,407,604)	142	142	215	

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR
Statistical analysis description:	
Week 2: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.396
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.44

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR
Statistical analysis description:	
Week 2: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5932
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.2

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 4: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3326
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.46

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 4: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1765
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.08

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 8: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5619
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.08

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.39

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 8: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3909
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.16

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 12: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7562
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.35

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 12: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.9476
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.31

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 16: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7746
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.36

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 16: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.6377
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.94

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.23

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 24: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8532
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.33

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 24: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5644
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.4

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 32: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.769
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.04
Confidence interval	
level	Other: 0.77 %
sides	2-sided
lower limit	0.8
upper limit	1.35

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 32: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4321
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.44

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 40: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7714
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.04

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.35

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 40: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8389
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.34

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 48: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.9383
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.29

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 48: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.88
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.33

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 56: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7946
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.26

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 56: Odds ratio and 95% CI estimated from logistic regression model. Logistic regression model included baseline LBPI and treatment.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7803
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.96

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.25

Secondary: Number of Subjects Who Took Rescue Medication During Week 64: Observed Data

End point title	Number of Subjects Who Took Rescue Medication During Week 64: Observed Data[37]

End point description:

In case of inadequate pain relief, after Week 24, acetaminophen/paracetamol up to 4000 mg per day up to 5 days in a week could be taken as rescue medication and use was reported weekly via diary. Number of subjects with any use of rescue medication during the 4 weeks up to and including the particular study week were summarized. ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo). Here, 'N' signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 64

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	60		
Units: subjects	35	26		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Days of Rescue Medication Used at Weeks 2, 4, 8, 12, 16, 24, 32, 40, 48 and 56

End point title	Number of Days of Rescue Medication Used at Weeks 2, 4, 8, 12, 16, 24, 32, 40, 48 and 56[38]

End point description:

In case of inadequate pain relief, acetaminophen/paracetamol caplets, tablets, or capsules up to 3000 mg per day up to 3 days in a week could be taken as rescue medication between day 1 and week 56. Number of days the subjects used the rescue medication during the particular study weeks were summarized. For analyses after week 16 where multiple imputation was used, data was reported per 3 arms. This is because subjects who received placebo from Day 1 and received tanezumab 5/10 mg at week 16, received placebo for the first 16 weeks, and their data before week 16 were not be imputed into analyses after week 16. ITT population included all randomized subjects who received at least one dose of SC study medication (either tanezumab or matching placebo).

End point type	Secondary

End point timeframe:

Weeks 2, 4, 8, 12, 16, 24, 32, 40, 48 and 56

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Tramadol PR	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	407	407	605	
Units: days				
least squares mean (standard error)				
Week 2	2.05 (± 0.15)	1.85 (± 0.14)	1.76 (± 0.11)	
Week 4	1.62 (± 0.13)	1.40 (± 0.12)	1.46 (± 0.10)	
Week 8	1.40 (± 0.13)	1.15 (± 0.11)	1.23 (± 0.09)	
Week 12	1.25 (± 0.13)	1.02 (± 0.11)	1.11 (± 0.09)	
Week 16	1.18 (± 0.13)	0.96 (± 0.11)	0.99 (± 0.09)	
Week 24	1.36 (± 0.15)	1.35 (± 0.14)	1.32 (± 0.12)	
Week 32	1.35 (± 0.15)	1.36 (± 0.15)	1.38 (± 0.12)	
Week 40	1.39 (± 0.15)	1.24 (± 0.14)	1.37 (± 0.12)	
Week 48	1.32 (± 0.14)	1.25 (± 0.14)	1.37 (± 0.12)	
Week 56	1.32 (± 0.14)	1.22 (± 0.13)	1.42 (± 0.12)	

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 2: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1272
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.41
Variability estimate	Standard error of the mean
Dispersion value	0.11

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 2: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.6322
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.27
Variability estimate	Standard error of the mean
Dispersion value	0.1

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 4: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3559
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.36
Variability estimate	Standard error of the mean
Dispersion value	0.12

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 4: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.6798
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.18

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR
Statistical analysis description:	
Week 8: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.267
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.44

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR
Statistical analysis description:	
Week 8: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5865
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.94

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.19

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR
Statistical analysis description:	
Week 12: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3378
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.47

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR
Statistical analysis description:	
Week 12: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.551
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.2

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 16: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2088
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.6
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 16: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8692
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 24: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8444
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.35
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 24: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8936
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.34
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 32: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8716
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.98

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.28
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR
Statistical analysis description:	
Week 32: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8827
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.29
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR
Statistical analysis description:	
Week 40: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8996
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.34
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR
Statistical analysis description: Week 40: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.488
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	0.13

Statistical analysis title	Tanezumab 5 mg versus Tramadol PR
Statistical analysis description: Week 48: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7938
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.27
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR
Statistical analysis description: Week 48: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5092
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	0.13

Statistical analysis title	Tanezumab 5 mg VersusTramadol PR

Statistical analysis description:

Week 56: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.6148
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.22
Variability estimate	Standard error of the mean
Dispersion value	0.13

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 56: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2844
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.13
Variability estimate	Standard error of the mean
Dispersion value	0.12

Secondary: Number of Days of Rescue Medication Used at Week 64

End point title	Number of Days of Rescue Medication Used at Week 64[39]

End point description:

In case of inadequate pain relief, acetaminophen/paracetamol caplets, tablets, or capsules up to 3000 mg per day up to 3 days in a week could be taken as rescue medication between day 1 and week 56. Number of days per week the subjects used the rescue medication during the 4 weeks up to and including the particular study week were summarized. ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo). Here, 'N' signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 64

Notes:

[39] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	60	136	151
Units: days				
arithmetic mean (standard deviation)	1.3 (± 1.59)	1.3 (± 2.02)	1.3 (± 1.99)	1.4 (± 2.16)

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	193			
Units: days				
arithmetic mean (standard deviation)	1.8 (± 2.44)			

Statistical analyses

No statistical analyses for this end point

Secondary: Amount of Rescue Medication Used at Weeks 2, 4, 8, 12 and 16

End point title	Amount of Rescue Medication Used at Weeks 2, 4, 8, 12 and

End point description:

In case of inadequate pain relief, acetaminophen/paracetamol up to 4000 mg per day up to 5 days in a week could be taken as rescue medication. The total dosage of acetaminophen in milligrams used during the specified week were summarized.
ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo).

End point type	Secondary

End point timeframe:

Weeks 2, 4, 8, 12 and 16

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: milligrams				
least squares mean (standard error)				
Week 2	2663.2 (± 431.26)	2465.7 (± 398.76)	2420.1 (± 392.67)	2340.4 (± 310.28)
Week 4	1967.2 (± 352.25)	1847.9 (± 330.64)	2084.6 (± 374.33)	1852.2 (± 271.70)
Week 8	1682.3 (± 338.34)	1612.5 (± 323.86)	1757.9 (± 354.02)	1512.4 (± 248.85)
Week 12	1491.6 (± 330.87)	1345.3 (± 297.82)	1707.2 (± 379.30)	1464.2 (± 265.85)
Week 16	1537.8 (± 377.76)	1359.0 (± 333.62)	1385.0 (± 340.93)	1296.8 (± 260.75)

Statistical analyses

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

Week 2: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Tanezumab 5 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.6764
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.73
Variability estimate	Standard error of the mean
Dispersion value	0.25

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

Week 2: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.9351
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.6
Variability estimate	Standard error of the mean
Dispersion value	0.23

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 2: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8731
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.97

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.46
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 2: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.537
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.72
Variability estimate	Standard error of the mean
Dispersion value	0.24

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

Week 2: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8031
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.59
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo
Statistical analysis description: Week 4: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8192
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.55
Variability estimate	Standard error of the mean
Dispersion value	0.24

Statistical analysis title	Pooled Placebo Versus Tanezumab 10 mg
Statistical analysis description: Week 4: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.6345
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.46
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	Pooled Placebo Versus Tramadol PR
Statistical analysis description: Week 4: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.6103
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	1.4
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 4: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7949
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.67
Variability estimate	Standard error of the mean
Dispersion value	0.25

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

Week 4: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Tanezumab 10 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.992
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.57
Variability estimate	Standard error of the mean
Dispersion value	0.23

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo
Statistical analysis description:	
Week 8: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8772
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.67
Variability estimate	Standard error of the mean
Dispersion value	0.27

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo
Statistical analysis description:	
Week 8: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7614
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.92

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.6
Variability estimate	Standard error of the mean
Dispersion value	0.26

Statistical analysis title	Pooled Placebo Versus Tramadol PR
Statistical analysis description:	
Week 8: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5629
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	1.43
Variability estimate	Standard error of the mean
Dispersion value	0.22

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR
Statistical analysis description:	
Week 8: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.6821
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.85
Variability estimate	Standard error of the mean
Dispersion value	0.29

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR
Statistical analysis description: Week 8: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8049
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.77
Variability estimate	Standard error of the mean
Dispersion value	0.28

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo
Statistical analysis description: Week 12: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.6673
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	1.62
Variability estimate	Standard error of the mean
Dispersion value	0.27

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo
Statistical analysis description: Week 12: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4475
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	1.46
Variability estimate	Standard error of the mean
Dispersion value	0.25

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

Week 12: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5925
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	0.25

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

Week 12: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.9486
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	1.79
Variability estimate	Standard error of the mean
Dispersion value	0.29

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR
Statistical analysis description:	
Week 12: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7673
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	1.61
Variability estimate	Standard error of the mean
Dispersion value	0.26

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo
Statistical analysis description:	
Week 16: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.7635
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.11

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	2.2
Variability estimate	Standard error of the mean
Dispersion value	0.39

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo
Statistical analysis description:	
Week 16: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.9564
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.94
Variability estimate	Standard error of the mean
Dispersion value	0.34

Statistical analysis title	Pooled Placebo Versus Tramadol PR
Statistical analysis description:	
Week 16: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8359
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.75
Variability estimate	Standard error of the mean
Dispersion value	0.3

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR
Statistical analysis description: Week 16: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5914
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	2.21
Variability estimate	Standard error of the mean
Dispersion value	0.38

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR
Statistical analysis description: Week 16: Analysis was performed using negative binomial model with model terms of Baseline average LBPI and treatment group.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8826
Method	Negative binomial model
Parameter estimate	LS Mean Ratio
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	1.95
Variability estimate	Standard error of the mean
Dispersion value	0.33

Secondary: Health Care Resource Utilization (HCRU): Number of Visits of Services Received Directly Related to Low Back Pain

End point title	Health Care Resource Utilization (HCRU): Number of Visits of Services Received Directly Related to Low Back Pain[41]

End point description:

Low back pain HCRU assessed utilization of healthcare resources usage during last 3 months (for Baseline during the last 3 months for baseline, weeks 64 and 80, via IRT). Visits of services directly related to low back pain evaluated were: visits to primary care physician, neurologist, rheumatologist, physician assistant or nurse practitioner, pain specialist, orthopedist, physical therapist, chiropractor, alternative medicine or therapy, podiatrist, nutritionist/dietitian, radiologist, home healthcare services and other practitioner. Subjects might have been counted more than once under various categories.ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo). Here, "n" subjects evaluable for OM at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 64 and 80

Notes:

[41] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: visits				
median (full range (min-max))				
Baseline: Primary Care Physician	1.0 (1.0 to 8.0)	2.0 (1.0 to 114.0)	2.0 (1.0 to 111.0)	2.0 (1.0 to 14.0)
Baseline: Neurologist	1.0 (1.0 to 2.0)	1.0 (1.0 to 3.0)	1.0 (1.0 to 2.0)	1.0 (1.0 to 6.0)
Baseline: Rheumatologist	2.0 (1.0 to 2.0)	1.0 (1.0 to 3.0)	2.0 (1.0 to 5.0)	1.0 (1.0 to 3.0)
Baseline:Physician assistant or nurse Practitioner	1.0 (1.0 to 6.0)	2.0 (1.0 to 10.0)	1.0 (1.0 to 5.0)	1.0 (1.0 to 6.0)
Baseline: Pain specialist	2.0 (1.0 to 22.0)	2.0 (1.0 to 25.0)	2.0 (1.0 to 30.0)	2.0 (1.0 to 222.0)
Baseline: Orthopedist	3.0 (1.0 to 8.0)	3.0 (1.0 to 36.0)	3.0 (1.0 to 15.0)	2.0 (1.0 to 12.0)
Baseline: Physical therapist	6.5 (1.0 to 24.0)	8.0 (1.0 to 36.0)	4.5 (1.0 to 20.0)	5.5 (1.0 to 111.0)
Baseline: Chiropractor	3.0 (1.0 to 10.0)	3.0 (1.0 to 36.0)	3.5 (1.0 to 30.0)	3.0 (1.0 to 24.0)
Baseline: Alternative medicine or therapy	2.0 (1.0 to 10.0)	2.0 (1.0 to 121.0)	3.0 (1.0 to 111.0)	2.0 (1.0 to 45.0)
Baseline: Podiatrist	2.0 (1.0 to 3.0)	99999 (99999 to 99999)	2.0 (1.0 to 3.0)	1.0 (1.0 to 2.0)
Baseline: Nutritionist/dietitian	99999 (99999 to 99999)	3.0 (1.0 to 100.0)	1.5 (1.0 to 6.0)	2.0 (1.0 to 4.0)
Baseline: Radiologist	1.0 (1.0 to 3.0)	1.5 (1.0 to 3.0)	1.0 (1.0 to 6.0)	1.0 (1.0 to 10.0)
Baseline: Home healthcare services	7.5 (3.0 to 12.0)	6.0 (1.0 to 11.0)	99999 (99999 to 99999)	1.0 (1.0 to 3.0)
Baseline: Other practitioner	1.0 (1.0 to 6.0)	2.0 (1.0 to 90.0)	1.0 (1.0 to 8.0)	2.0 (1.0 to 111.0)
Week 64: Primary Care Physician	1.0 (1.0 to 5.0)	1.0 (1.0 to 299.0)	1.0 (1.0 to 211.0)	1.0 (1.0 to 201.0)
Week 64: Neurologist	1.0 (1.0 to 18.0)	1.5 (1.0 to 3.0)	1.0 (1.0 to 4.0)	1.5 (1.0 to 3.0)
Week 64: Rheumatologist	2.0 (1.0 to 14.0)	1.0 (1.0 to 27.0)	1.0 (1.0 to 100.0)	1.0 (1.0 to 101.0)
Week 64: Physician assistant or nurse Practitioner	1.0 (1.0 to 201.0)	1.0 (1.0 to 8.0)	2.0 (1.0 to 6.0)	1.0 (1.0 to 3.0)

Week 64: Pain specialist	1.0 (1.0 to 16.0)	2.0 (1.0 to 100.0)	2.0 (1.0 to 10.0)	1.0 (1.0 to 201.0)
Week 64: Orthopedist	2.0 (1.0 to 9.0)	1.5 (1.0 to 27.0)	1.0 (1.0 to 6.0)	1.0 (1.0 to 201.0)
Week 64: Physical therapist	10.0 (1.0 to 18.0)	8.0 (1.0 to 36.0)	4.5 (1.0 to 20.0)	4.0 (1.0 to 30.0)
Week 64: Chiropractor	6.0 (1.0 to 36.0)	2.5 (1.0 to 100.0)	2.0 (1.0 to 25.0)	3.5 (1.0 to 92.0)
Week 64: Alternative medicine or therapy	6.0 (1.0 to 300.0)	1.0 (1.0 to 2.0)	2.0 (1.0 to 24.0)	1.0 (1.0 to 5.0)
Week 64: Podiatrist	1.5 (1.0 to 2.0)	2.0 (1.0 to 3.0)	1.0 (1.0 to 2.0)	1.0 (1.0 to 2.0)
Week 64: Nutritionist/dietitian	99999 (99999 to 99999)	1.0 (1.0 to 100.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)
Week 64: Radiologist	1.0 (1.0 to 3.0)	1.5 (1.0 to 3.0)	1.0 (1.0 to 2.0)	1.0 (1.0 to 1.0)
Week 64: Home healthcare services	8.0 (8.0 to 8.0)	3.0 (1.0 to 5.0)	1.0 (1.0 to 1.0)	2.0 (1.0 to 3.0)
Week 64: Other practitioner	1.0 (1.0 to 18.0)	2.0 (1.0 to 100.0)	1.0 (1.0 to 111.0)	1.0 (1.0 to 16.0)
Week 80: Primary Care Physician	2.0 (1.0 to 3.0)	1.0 (1.0 to 36.0)	1.0 (1.0 to 101.0)	1.0 (1.0 to 4.0)
Week 80: Neurologist	1.0 (1.0 to 1.0)	2.0 (2.0 to 2.0)	2.5 (2.0 to 3.0)	2.0 (2.0 to 2.0)
Week 80: Rheumatologist	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 2.0)	1.0 (1.0 to 1.0)
Week 80: Physician assistant or nurse Practitioner	5.0 (1.0 to 9.0)	50.5 (1.0 to 100.0)	1.0 (1.0 to 3.0)	1.0 (1.0 to 1.0)
Week 80: Pain specialist	2.0 (1.0 to 2.0)	1.0 (1.0 to 11.0)	2.5 (1.0 to 4.0)	1.0 (1.0 to 3.0)
Week 80: Orthopedist	1.0 (1.0 to 2.0)	2.0 (1.0 to 6.0)	1.0 (1.0 to 3.0)	1.5 (1.0 to 2.0)
Week 80: Physical therapist	5.0 (1.0 to 8.0)	12.0 (1.0 to 20.0)	4.0 (1.0 to 16.0)	5.0 (1.0 to 20.0)
Week 80: Chiropractor	401.0 (1.0 to 801.0)	3.5 (1.0 to 9.0)	4.0 (1.0 to 10.0)	4.0 (1.0 to 20.0)
Week 80: Alternative medicine or therapy	9.0 (3.0 to 15.0)	2.5 (1.0 to 30.0)	3.0 (1.0 to 4.0)	2.5 (2.0 to 3.0)
Week 80: Podiatrist	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)
Week 80: Nutritionist/dietitian	1.0 (1.0 to 1.0)	10.0 (10.0 to 10.0)	1.0 (1.0 to 1.0)	4.0 (2.0 to 6.0)
Week 80: Radiologist	1.0 (1.0 to 1.0)	99999 (99999 to 99999)	1.5 (1.0 to 2.0)	1.0 (1.0 to 2.0)
Week 80: Home healthcare services	1.0 (1.0 to 1.0)	99999 (99999 to 99999)	4.0 (4.0 to 4.0)	99999 (99999 to 99999)
Week 80: Other practitioner	1.0 (1.0 to 11.0)	1.0 (1.0 to 2.0)	1.0 (1.0 to 4.0)	1.0 (1.0 to 3.0)

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: visits				
median (full range (min-max))				
Baseline: Primary Care Physician	2.0 (1.0 to 562.0)			
Baseline: Neurologist	1.0 (1.0 to 4.0)			
Baseline: Rheumatologist	1.0 (1.0 to 6.0)			
Baseline:Physician assistant or nurse Practitioner	1.0 (1.0 to 6.0)			
Baseline: Pain specialist	2.0 (1.0 to 11.0)			

Baseline: Orthopedist	3.0 (1.0 to 16.0)			
Baseline: Physical therapist	3.5 (1.0 to 90.0)			
Baseline: Chiropractor	3.0 (1.0 to 121.0)			
Baseline: Alternative medicine or therapy	2.0 (1.0 to 211.0)			
Baseline: Podiatrist	1.0 (1.0 to 1.0)			
Baseline: Nutritionist/dietitian	1.0 (1.0 to 1.0)			
Baseline: Radiologist	1.0 (1.0 to 4.0)			
Baseline: Home healthcare services	6.5 (1.0 to 36.0)			
Baseline: Other practitioner	1.0 (1.0 to 36.0)			
Week 64: Primary Care Physician	1.0 (1.0 to 200.0)			
Week 64: Neurologist	1.0 (1.0 to 101.0)			
Week 64: Rheumatologist	1.0 (1.0 to 2.0)			
Week 64: Physician assistant or nurse Practitioner	1.0 (1.0 to 3.0)			
Week 64: Pain specialist	1.0 (1.0 to 4.0)			
Week 64: Orthopedist	2.0 (1.0 to 100.0)			
Week 64: Physical therapist	3.0 (1.0 to 999.0)			
Week 64: Chiropractor	2.0 (1.0 to 999.0)			
Week 64: Alternative medicine or therapy	1.0 (1.0 to 111.0)			
Week 64: Podiatrist	1.0 (1.0 to 1.0)			
Week 64: Nutritionist/dietitian	1.0 (1.0 to 9.0)			
Week 64: Radiologist	1.0 (1.0 to 2.0)			
Week 64: Home healthcare services	16.5 (1.0 to 401.0)			
Week 64: Other practitioner	1.0 (1.0 to 6.0)			
Week 80: Primary Care Physician	1.0 (1.0 to 12.0)			
Week 80: Neurologist	2.0 (1.0 to 3.0)			
Week 80: Rheumatologist	1.0 (1.0 to 1.0)			
Week 80: Physician assistant or nurse Practitioner	2.0 (2.0 to 2.0)			
Week 80: Pain specialist	1.0 (1.0 to 3.0)			
Week 80: Orthopedist	1.5 (1.0 to 7.0)			
Week 80: Physical therapist	6.0 (6.0 to 14.0)			
Week 80: Chiropractor	3.0 (1.0 to 14.0)			
Week 80: Alternative medicine or therapy	2.0 (1.0 to 5.0)			
Week 80: Podiatrist	1.5 (1.0 to 2.0)			
Week 80: Nutritionist/dietitian	99999 (99999 to 99999)			
Week 80: Radiologist	1.0 (1.0 to 1.0)			
Week 80: Home healthcare services	24.5 (13.0 to 36.0)			
Week 80: Other practitioner	1.0 (1.0 to 10.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Resource Utilization (HCRU): Number of Subjects who Visited the Emergency Room Due to Low Back Pain

End point title	Health Care Resource Utilization (HCRU): Number of Subjects who Visited the Emergency Room Due to Low Back Pain[42]

End point description:

Low back pain HCRU assessed utilization of healthcare resources during the last 3 months for baseline, weeks 64 and 80, via IRT. Domain evaluated was number of subjects who visited the emergency room due to low back pain. ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo). Here, "n" subjects evaluable for OM at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 64 and 80

Notes:

[42] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: subjects				
Baseline(n=202,204,407,407,605)	10	14	27	17
Week 64(n=135, 138, 285,285,414)	4	2	7	5
Week 80(n= 61, 59,134, 143, 191)	0	3	3	0

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: subjects				
Baseline(n=202,204,407,407,605)	26			
Week 64(n=135, 138, 285,285,414)	3			
Week 80(n= 61, 59,134, 143, 191)	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Resource Utilization (HCRU): Number of Visits to the Emergency Room Due to Low Back Pain

End point title	Health Care Resource Utilization (HCRU): Number of Visits to the Emergency Room Due to Low Back Pain[43]

End point description:

Low back pain HCRU assessed utilization of healthcare resources during the last 3 months for baseline, weeks 64 and 80, via IRT. Domain evaluated was number of visits to the emergency room due to low back pain. ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo). Not all subjects of the ITT population had data collected at each of the time points for this end point. Here, "n" subjects evaluable for end point at specified time points and 99999 signifies that no data evaluable.

End point type	Secondary

End point timeframe:

Baseline, Weeks 64 and 80

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: visits				
median (full range (min-max))				
Baseline(n=10, 14, 27, 17, 26)	1.0 (1.0 to 3.0)	1.0 (1.0 to 6.0)	1.0 (1.0 to 4.0)	1.0 (1.0 to 5.0)
Week 64(n=4, 2, 7, 5, 3)	1.0 (1.0 to 1.0)	2.0 (2.0 to 2.0)	1.0 (1.0 to 3.0)	1.0 (1.0 to 6.0)
Week 80(n= 0, 3, 3, 0, 4)	99999 (99999 to 99999)	1.0 (1.0 to 11.0)	1.0 (1.0 to 2.0)	99999 (99999 to 99999)

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: visits				
median (full range (min-max))				
Baseline(n=10, 14, 27, 17, 26)	1.0 (1.0 to 7.0)			
Week 64(n=4, 2, 7, 5, 3)	1.0 (1.0 to 2.0)			
Week 80(n= 0, 3, 3, 0, 4)	1.5 (1.0 to 2.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Resource Utilization (HCRU): Number of Subjects Hospitalized Due to Low Back Pain

End point title	Health Care Resource Utilization (HCRU): Number of Subjects Hospitalized Due to Low Back Pain[44]

End point description:

Low back pain HCRU assessed utilization of healthcare resources during the last 3 months for baseline, weeks 64 and 80, via IRT. Domain evaluated was number of subjects who were hospitalized due to low back pain. ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo). Here, 'n'= subjects evaluable for this end point at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 64 and 80

Notes:

[44] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: subjects				
Baseline(n=202, 204, 406,407,605)	0	0	1	0
Week 64(n=135,138,285,285,413)	0	0	0	1
Week 80(n=61, 59,134,143,191)	0	1	1	0

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: subjects				
Baseline(n=202, 204, 406,407,605)	4			
Week 64(n=135,138,285,285,413)	1			
Week 80(n=61, 59,134,143,191)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Resource Utilization (HCRU): Number of Nights Stayed in the Hospital Due to Low Back Pain

End point title	Health Care Resource Utilization (HCRU): Number of Nights Stayed in the Hospital Due to Low Back Pain[45]

End point description:

Low back pain HCRU assessed utilization of healthcare resources during the last 3 months for baseline, weeks 64 and 80, via IRT. Domain evaluated was number of nights stayed in the hospital due to low back pain. ITT population included all randomized subjects who received at least 1 dose of SC study

medication (either tanezumab or matching placebo). Not all subjects of the ITT population had data collected at each of the time points for this endpoint. Here, 'n'= subjects evaluable for this end point at specified time points and 99999 signifies that no data evaluable.

End point type	Secondary

End point timeframe:

Baseline, Weeks 64 and 80

Notes:

[45] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: nights				
median (full range (min-max))				
Baseline(n=0, 0, 1, 0, 4)	99999 (99999 to 99999)	99999 (99999 to 99999)	9.0 (9.0 to 9.0)	99999 (99999 to 99999)
Week 64(n=0, 0, 0, 1, 1)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	1.0 (1.0 to 1.0)
Week 80(n= 0, 1, 1, 0, 1)	99999 (99999 to 99999)	3.0 (3.0 to 3.0)	2.0 (2.0 to 2.0)	99999 (99999 to 99999)

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: nights				
median (full range (min-max))				
Baseline(n=0, 0, 1, 0, 4)	1.0 (1.0 to 2.0)			
Week 64(n=0, 0, 0, 1, 1)	1.0 (1.0 to 1.0)			
Week 80(n= 0, 1, 1, 0, 1)	2.0 (2.0 to 2.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Resource Utilization (HCRU): Number of Subjects who Used Any Aids/Devices for Doing Things

End point title	Health Care Resource Utilization (HCRU): Number of Subjects who Used Any Aids/Devices for Doing Things[46]

End point description:

Low back pain HCRU assessed utilization of healthcare resources during the last 3 months for baseline, weeks 64 and 80, via IRT. Domain evaluated was number of subjects who used any aids/devices for doing things. Aids such as walking aid, wheelchair, device or utensil for dress/bathe/eat and any other aids/devices. ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo).

End point type	Secondary

End point timeframe:

Baseline, Weeks 64 and 80

Notes:

[46] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: subjects				
Baseline:Walking aid useNever	186	190	376	371
Baseline:Wheelchair useNever	199	204	403	405
Baseline:Device/Utensil to dress bathe eatNever	192	196	390	396
Baseline:Other aids or devicesNever	188	188	387	382
Week 64:Walking aid useNever	125	131	277	273
Week 64:Wheelchair useNever	135	138	283	283
Week 64:Device/Utensil to dress bathe eatNever	134	137	283	280
Week 64:Other aids or devicesNever	125	135	277	273
Week 80:Walking aid useNever	55	56	130	141
Week 80:Wheelchair useNever	61	59	134	142
Week 80:Device/Utensil to dress bathe eatNever	60	57	132	142
Week 80:Other aids or devicesNever	57	58	128	139
Baseline:Walking aid useRarely	2	2	11	9
Baseline:Wheelchair useRarely	1	0	3	0
Baseline:Device/Utensil to dress bathe eatRarely	0	1	1	1
Baseline:Other aids or devicesRarely	1	2	2	5
Week 64:Walking aid useRarely	2	4	1	3
Week 64:Wheelchair useRarely	0	0	1	1
Week 64:Device/Utensil to dress bathe eatRarely	0	0	0	2
Week 64:Other aids or devicesRarely	1	1	0	0
Week 80:Walking aid useRarely	0	0	1	1
Week 80:Wheelchair useRarely	0	0	0	1
Week 80:Device/Utensil to dress bathe eatRarely	0	1	0	1
Week 80:Other aids or devicesRarely	1	1	1	1
Baseline:Walking aid useSometimes	6	4	12	16
Baseline:Wheelchair useSometimes	2	0	0	2
Baseline:Device/Utensil todress bathe eatSometimes	4	3	6	4
Baseline:Other aids or devicesSometimes	2	5	10	11
Week 64:Walking aid useSometimes	5	1	2	5
Week 64:Wheelchair useSometimes	0	0	1	0
Week 64:DeviceUtensil to dress bathe eatSometimes	0	0	2	3

Week 64:Other aids or devicesSometimes	5	1	5	7
Week 80:Walking aid useSometimes	3	1	1	1
Week 80:Wheelchair useSometimes	0	0	0	0
Week 80:Device/Utensil to dress bathe eatSometimes	1	1	0	0
Week 80:Other aids or devicesSometimes	1	0	1	3
Baseline:Walking aid useOften	6	5	4	7
Baseline:Wheelchair useOften	0	0	0	0
Baseline:DeviceUtensil to dress bathe eat|Often	5	1	6	3
Baseline:Other aids or devicesOften	10	5	4	6
Week 64:Walking aid useOften	1	0	3	3
Week 64:Wheelchair useOften	0	0	0	0
Week 64:Device/Utensil to dress bathe eatOften	0	1	0	0
Week 64:Other aids or devicesOften	2	1	1	3
Week 80:Walking aid useOften	2	1	1	0
Week 80:Wheelchair useOften	0	0	0	0
Week80:Device/Utensil to dress bathe eatOften	0	0	1	0
Week 80:Other aids or devicesOften	2	0	1	0
Baseline:Walking aid useAlways	2	3	3	4
Baseline: Wheelchair useAlways	0	0	0	0
Baseline:Device/Utensil to dress bathe eatAlways	1	3	3	3
Baseline:Other aids or devicesAlways	1	4	3	3
Week 64:Walking aid useAlways	2	2	2	1
Week 64: Wheelchair useAlways	0	0	0	1
Week64:Device/Utensil to dress bathe eatAlways	1	0	0	0
Week 64:Other aids or devicesAlways	2	0	2	2
Week 80: Walking aid useAlways	1	1	1	0
Week 80: Wheelchair useAlways	0	0	0	0
Week80:Device/Utensil to dress bathe eatAlways	0	0	1	0
Week80:Other aids or devicesAlways	0	0	3	0

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: subjects				
Baseline:Walking aid useNever	569			
Baseline:Wheelchair useNever	601			
Baseline:Device/Utensil to dress bathe eatNever	596			
Baseline:Other aids or devicesNever	550			
Week 64:Walking aid useNever	397			
Week 64:Wheelchair useNever	412			
Week 64:Device/Utensil to dress bathe eatNever	410			

Week 64:Other aids or devicesNever	387			
Week 80:Walking aid useNever	182			
Week 80:Wheelchair useNever	190			
Week 80:Device/Utensil to dress bathe eatNever	190			
Week 80:Other aids or devicesNever	184			
Baseline:Walking aid useRarely	7			
Baseline:Wheelchair useRarely	1			
Baseline:Device/Utensil to dress bathe eatRarely	0			
Baseline:Other aids or devicesRarely	8			
Week 64:Walking aid useRarely	3			
Week 64:Wheelchair useRarely	0			
Week 64:Device/Utensil to dress bathe eatRarely	0			
Week 64:Other aids or devicesRarely	9			
Week 80:Walking aid useRarely	2			
Week 80:Wheelchair useRarely	0			
Week 80:Device/Utensil to dress bathe eatRarely	1			
Week 80:Other aids or devicesRarely	0			
Baseline:Walking aid useSometimes	15			
Baseline:Wheelchair useSometimes	3			
Baseline:Device/Utensil todress bathe eatSometimes	4			
Baseline:Other aids or devicesSometimes	27			
Week 64:Walking aid useSometimes	9			
Week 64:Wheelchair useSometimes	1			
Week 64:DeviceUtensil to dress bathe eatSometimes	2			
Week 64:Other aids or devicesSometimes	8			
Week 80:Walking aid useSometimes	4			
Week 80:Wheelchair useSometimes	0			
Week 80:Device/Utensil to dress bathe eatSometimes	0			
Week 80:Other aids or devicesSometimes	3			
Baseline:Walking aid useOften	9			
Baseline:Wheelchair useOften	0			
Baseline:DeviceUtensil to dress bathe eat|Often	4			
Baseline:Other aids or devicesOften	17			
Week 64:Walking aid useOften	2			
Week 64:Wheelchair useOften	1			
Week 64:Device/Utensil to dress bathe eatOften	0			
Week 64:Other aids or devicesOften	7			
Week 80:Walking aid useOften	2			
Week 80:Wheelchair useOften	0			
Week80:Device/Utensil to dress bathe eatOften	0			
Week 80:Other aids or devicesOften	2			
Baseline:Walking aid useAlways	5			
Baseline: Wheelchair useAlways	0			

Baseline:Device/Utensil to dress bathe eatAlways	1			
Baseline:Other aids or devicesAlways	3			
Week 64:Walking aid useAlways	3			
Week 64: Wheelchair useAlways	0			
Week64:Device/Utensil to dress bathe eatAlways	2			
Week 64:Other aids or devicesAlways	3			
Week 80: Walking aid useAlways	1			
Week 80: Wheelchair useAlways	1			
Week80:Device/Utensil to dress bathe eatAlways	0			
Week80:Other aids or devicesAlways	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Resource Utilization (HCRU): Number of Subjects who Quit Job Due to Low Back Pain

End point title	Health Care Resource Utilization (HCRU): Number of Subjects who Quit Job Due to Low Back Pain[47]

End point description:

Low back pain HCRU assessed utilization of healthcare resources during the last 3 months for baseline, weeks 64 and 80, via IRT. Domain evaluated was number of subjects who quit job due to low back pain. ITT population included all randomized subjects who received at least 1 dose of SC study medication (either tanezumab or matching placebo). Here, 'n'= subjects evaluable for this end point at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 64 and 80

Notes:

[47] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: subjects				
Baseline(n= 17, 15, 28, 31, 47)	17	14	28	31
Week 64(n= 6, 3, 14, 10, 21)	6	2	11	8
Week 80(n= 4, 2, 4, 3, 3)	4	2	4	3

End point values	Tramadol PR			

Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: subjects				
Baseline(n= 17, 15, 28, 31, 47)	47			
Week 64(n= 6, 3, 14, 10, 21)	14			
Week 80(n= 4, 2, 4, 3, 3)	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Resource Utilization (HCRU): Duration Since Quitting Job Due to Low Back Pain

End point title	Health Care Resource Utilization (HCRU): Duration Since Quitting Job Due to Low Back Pain[48]

End point description:

Low back pain HCRU assessed utilization of healthcare resources during the last 3 months for baseline, weeks 64 and 80, via IRT. Domain evaluated was duration since quitting job due to low back pain. ITT population. Not all subjects of the ITT population had data collected at each of the time points for this endpoint. Hence, "N" signifies only those subjects who were evaluable for this endpoint. Additional subjects apart from the ones who had responded for quitting job responded to duration since quitting job.

End point type	Secondary

End point timeframe:

Baseline, Weeks 64 and 80

Notes:

[48] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo Followed by Tanezumab 5 mg	Placebo Followed by Tanezumab 10 mg	Tanezumab 5 mg	Tanezumab 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	202	204	407	407
Units: years				
median (full range (min-max))				
Baseline	2.0 (0.2 to 15.0)	2.0 (0.3 to 15.6)	1.0 (0.1 to 20.5)	3.8 (0.1 to 16.0)
Week 64	1.1 (0.1 to 13.2)	5.2 (2.5 to 7.1)	2.2 (0.2 to 32.0)	2.0 (0.1 to 17.0)
Week 80	8.6 (5.8 to 99.1)	4.7 (1.0 to 8.3)	0.2 (0.0 to 3.3)	3.5 (0.8 to 17.1)

End point values	Tramadol PR			
Subject group type	Subject analysis set			
Number of subjects analysed	605			
Units: years				
median (full range (min-max))				

Baseline	2.3 (0.1 to 90.3)			
Week 64	2.5 (0.1 to 25.2)			
Week 80	3.5 (3.0 to 5.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Satisfaction Score Determined With Treatment Satisfaction Questionnaire for Medication Version II (TSQM v II) at Weeks 16 and 56

End point title	Treatment Satisfaction Score Determined With Treatment Satisfaction Questionnaire for Medication Version II (TSQM v II) at Weeks 16 and 56[49]

End point description:

TSQM v.II: self-administered 11-item validated scale that quantified subject's level of satisfaction with study medication 11 questions of TSQM were used to calculate 4 endpoints of effectiveness, side effects, convenience and global satisfaction, each scored on a 0-100 scale with 100=best level of satisfaction. Pre-specified intent of study for efficacy data up to Week 16 was to analyze subject who received placebo from Day 1 and tanezumab 5/10 mg at week 16 in placebo arm. Hence data have been reported per 4 arms. ITT population was used. Pre-specified intent of study was to compare tanezumab Vs placebo for data up to & including W16 & comparisons of tanezumab Vs tramadol for data up to & including W56. Here, "N"=subjects evaluable for this endpoint. Data were not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16.

End point type	Secondary

End point timeframe:

Weeks 16 and 56

Notes:

[49] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: units on a scale				
least squares mean (standard error)				
Week16:Effectiveness(n= 338, 343, 329, 456)	63.69 (± 1.48)	62.87 (± 1.48)	56.67 (± 1.50)	61.39 (± 1.30)
Week16:Side Effects(n= 49, 49, 39, 120)	79.26 (± 3.31)	79.51 (± 3.31)	66.95 (± 3.76)	70.83 (± 2.15)
Week16:Convenience(n= 338, 343, 329, 456)	75.68 (± 1.16)	76.37 (± 1.15)	73.11 (± 1.16)	74.63 (± 1.04)
Week16:Global Satisfaction(n= 338, 343, 329, 456)	70.32 (± 1.39)	68.64 (± 1.38)	64.90 (± 1.41)	67.12 (± 1.22)
Week56:Effectiveness(n= 141, 159, 0, 206)	72.66 (± 2.12)	72.51 (± 2.01)	99999 (± 99999)	71.21 (± 1.79)
Week56:Side Effects(n= 9, 17, 0, 41)	78.92 (± 6.32)	89.37 (± 4.76)	99999 (± 99999)	76.20 (± 3.09)
Week56:Convenience(n= 141, 159, 0, 206)	78.72 (± 1.69)	80.52 (± 1.60)	99999 (± 99999)	78.42 (± 1.45)
Week56:Global Satisfaction(n= 141, 159, 0, 206)	78.11 (± 1.83)	78.49 (± 1.73)	99999 (± 99999)	74.57 (± 1.55)

Statistical analyses

Statistical analysis title	Pooled Placebo, Tanezumab 5 mg
Statistical analysis description:	
TSQM Effectiveness; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.	
Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0005
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	7.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.07
upper limit	10.97
Variability estimate	Standard error of the mean
Dispersion value	2.01

Statistical analysis title	Pooled Placebo Versus Tanezumab 10 mg
Statistical analysis description:	
TSQM Effectiveness; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.	
Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0021
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	6.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.26
upper limit	10.15
Variability estimate	Standard error of the mean
Dispersion value	2.01

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

TSQM Effectiveness; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0125
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	4.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	8.42
Variability estimate	Standard error of the mean
Dispersion value	1.89

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

TSQM Effectiveness; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2176
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.36
upper limit	5.97
Variability estimate	Standard error of the mean
Dispersion value	1.87

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

TSQM Effectiveness; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4235
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.16
upper limit	5.14
Variability estimate	Standard error of the mean
Dispersion value	1.86

Statistical analysis title	Tanezumab 5 mg Versus Pooled Placebo

Statistical analysis description:

TSQM Side Effects; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0143
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	12.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.5
upper limit	22.11
Variability estimate	Standard error of the mean
Dispersion value	4.96

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

TSQM Side Effects; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0124
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	12.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.76
upper limit	22.35
Variability estimate	Standard error of the mean
Dispersion value	4.96

Statistical analysis title	Pooled Placebo Versus Tramadol PR
Statistical analysis description:	
TSQM Side Effects; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.	
Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3675
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	3.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	12.36
Variability estimate	Standard error of the mean
Dispersion value	4.29

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR
Statistical analysis description:	
TSQM Side Effects; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0319
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	8.42

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	16.11
Variability estimate	Standard error of the mean
Dispersion value	3.89

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

TSQM Side Effects; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0276
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	8.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	16.38
Variability estimate	Standard error of the mean
Dispersion value	3.9

Statistical analysis title	Pooled Placebo Versus Tanezumab 5 mg

Statistical analysis description:

TSQM Convenience; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0627
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	5.27
Variability estimate	Standard error of the mean
Dispersion value	1.38

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo
Statistical analysis description:	
TSQM Convenience; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.	
Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0187
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	3.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	5.97
Variability estimate	Standard error of the mean
Dispersion value	1.38

Statistical analysis title	Pooled Placebo Versus Tramadol PR
Statistical analysis description:	
TSQM Convenience; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.	
Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2419
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.03
upper limit	4.06
Variability estimate	Standard error of the mean
Dispersion value	1.3

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR
Statistical analysis description:	
TSQM Convenience; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.	

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.4124
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.46
upper limit	3.56
Variability estimate	Standard error of the mean
Dispersion value	1.28

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

TSQM Convenience; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.173
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	4.24
Variability estimate	Standard error of the mean
Dispersion value	1.27

Statistical analysis title	Pooled Placebo Versus Tanezumab 5 mg

Statistical analysis description:

TSQM Global Satisfaction; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Placebo

Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0037
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	5.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.77
upper limit	9.08
Variability estimate	Standard error of the mean
Dispersion value	1.86

Statistical analysis title	Tanezumab 10 mg Versus Pooled Placebo

Statistical analysis description:

TSQM Global Satisfaction; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Placebo
Number of subjects included in analysis	813
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0449
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	3.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	7.39
Variability estimate	Standard error of the mean
Dispersion value	1.86

Statistical analysis title	Pooled Placebo Versus Tramadol PR

Statistical analysis description:

TSQM Global Satisfaction; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.

Comparison groups	Placebo v Tramadol PR
Number of subjects included in analysis	1011
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2038
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.22

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.21
upper limit	5.65
Variability estimate	Standard error of the mean
Dispersion value	1.75

Statistical analysis title	Pooled Placebo Versus Tramadol PR
Statistical analysis description:	
TSQM Global Satisfaction; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0644
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	6.59
Variability estimate	Standard error of the mean
Dispersion value	1.73

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR
Statistical analysis description:	
TSQM Global Satisfaction; Week 16: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.3775
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.86
upper limit	4.9
Variability estimate	Standard error of the mean
Dispersion value	1.72

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR
Statistical analysis description:	
TSQM Effectiveness; Week 56: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.	
Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.5806
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	6.6
Variability estimate	Standard error of the mean
Dispersion value	2.62

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR
Statistical analysis description:	
TSQM Effectiveness; Week 56: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.	
Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.6084
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.68
upper limit	6.6
Variability estimate	Standard error of the mean
Dispersion value	2.53

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR
Statistical analysis description:	
TSQM Side Effects; Week 56: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.	

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.6991
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.56
upper limit	16.99
Variability estimate	Standard error of the mean
Dispersion value	6.95

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

TSQM Side Effects; Week 56: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0265
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	13.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.66
upper limit	24.68
Variability estimate	Standard error of the mean
Dispersion value	5.6

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

TSQM Convenience; Week 56: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR

Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.8795
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.61
upper limit	4.21
Variability estimate	Standard error of the mean
Dispersion value	1.99

Statistical analysis title	Tanezumab 10 mg Versus Tramadol PR

Statistical analysis description:

TSQM Convenience; Week 56: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.2758
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.68
upper limit	5.87
Variability estimate	Standard error of the mean
Dispersion value	1.92

Statistical analysis title	Tanezumab 5 mg Versus Tramadol PR

Statistical analysis description:

TSQM Global Satisfaction; Week 56: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.

Comparison groups	Tanezumab 5 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.1197
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	3.54

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	8
Variability estimate	Standard error of the mean
Dispersion value	2.27

Statistical analysis title	Tanezumab 10 mg versus Tramadol PR

Statistical analysis description:

TSQM Global Satisfaction; Week 56: p-value was computed using ANCOVA with covariates of baseline average LBPI score, treatment, and study site as a random effect.

Comparison groups	Tanezumab 10 mg v Tramadol PR
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0743
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	3.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.39
upper limit	8.24
Variability estimate	Standard error of the mean
Dispersion value	2.19

Secondary: Patient Reported Treatment Impact Assessment-Modified (mPRTI) Score at Weeks 16 and 56: Subject Global Preference Assessment- What is The Current or Most Recent Treatment You Were Receiving For Low Back Pain Before Enrolling?

End point title	Patient Reported Treatment Impact Assessment-Modified (mPRTI) Score at Weeks 16 and 56: Subject Global Preference Assessment- What is The Current or Most Recent Treatment You Were Receiving For Low Back Pain Before Enrolling?[50]

End point description:

mPRTI:self-administered questionnaire containing subject reported treatment impact assessment, subject global preference assessment and subject willingness to use drug again assessment.Pre-specified intent of study for efficacy data up to W16 was to analyze, subjects received placebo from Day 1 and received tan 5/10 mg at week 16 in placebo arm, in pooled manner.Data have been reported per 4 arms.ITT population. Pre-specified intent of study was to compare tan Vs placebo for data up to and including week 16 and comparisons of tan Vs tramadol for data up to and including week 56. Hence, number analyzed is 0 for placebo arm for week 16 and onwards. Here "n" =subjects who were evaluable at specified time point. Data were not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16.

End point type	Secondary

End point timeframe:

Weeks 16 and 56

Notes:

[50] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: subjects				
Week16:InjectablePM(n= 333,340,322, 450)	21	22	20	39
Week56:InjectablePM(n=141, 159, 0, 206)	6	13	0	9
Week16:PMtaken by mouth(n= 333,340, 322,450)	211	229	213	287
Week56:PMtaken by mouth(n= 141, 159, 0, 206)	91	102	0	147
Week16:Surgery(n= 333,340,322, 450)	2	1	2	1
Week 56:Surgery(n= 141, 159, 0, 206)	2	0	0	3
Week 16:PM and surgery(n= 333,340,322,450)	9	10	7	14
Week 56:PM and surgery(n= 141, 159,0, 206)	7	4	0	3
Week 16:No treatment(n= 333,340, 322,450)	90	78	80	109
Week 56:No treatment(n= 141, 159, 0, 206)	35	40	0	44

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Reported Treatment Impact Assessment-Modified (mPRTI) Score at Weeks 16 and 56: Subject Global Preference Assessment- Overall, do You Prefer The Drug That You Received in This Study to Previous Treatment?

End point title	Patient Reported Treatment Impact Assessment-Modified (mPRTI) Score at Weeks 16 and 56: Subject Global Preference Assessment- Overall, do You Prefer The Drug That You Received in This Study to Previous Treatment?[51]

End point description:

mPRTI:self-administered questionnaire containing subject reported treatment impact assessment, subject GPA & subject willingness to use drug again assessment. Subjects responded using IRT on 5 point scale from 1-5,.Higher scores indicate lesser willingness to use the investigational product. Pre-specified intent of study for efficacy data up to Week 16 was to analyze, subjects who received placebo from Day 1 & received tan 5/10 mg at week 16 in placebo arm, in pooled manner. Data have been reported per 4 arms.ITT. Pre-specified intent of study was to compare tan Vs placebo for data up to and W16 and comparisons of tan Vs tramadol for data up to and including W56.Number analyzed is 0 for placebo arm for W16 and onwards. Here "n" =subjects evaluable at specified time point. '99999' =no subjects evaluable. Data were not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16.

End point type	Secondary

End point timeframe:

Weeks 16 and 56

Notes:

[51] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: subjects				
W16Yes surely prefer study drug(n=340,406,333,605)	172	191	150	232
W56Yes surely prefer study drug(n=141,159,0,206)	90	104	99999	129
W16Prefer slightly study drug(n=340,406,333,605)	62	50	57	89
W56Prefer slightly study drug(n =141,159,0,206)	30	36	99999	42
W16No preference either way(n =340, 406, 333, 605)	66	55	62	82
W56No preference either way(n =141, 159, 0, 206)	15	12	99999	22
W16Prefer slightly old drug(n=340,406,333,605)	14	23	24	17
W56Prefer slightly old drug(n =141, 159, 0, 206)	2	4	99999	7
W16No surely prefer old drug(n=340,406,333,605)	19	21	29	30
W56No surely prefer old drug(n=141,159,0,206)	4	3	99999	6

Statistical analyses

No statistical analyses for this end point

Secondary: Subject Reported Treatment Impact Assessment-Modified (mPRTI) Score at Weeks 16 and 56: Subject Willingness to Use Drug Again Assessment- Willing to Use The Same Drug That You Have Received in This Study For Your Low Back Pain Pain?

End point title	Subject Reported Treatment Impact Assessment-Modified (mPRTI) Score at Weeks 16 and 56: Subject Willingness to Use Drug Again Assessment- Willing to Use The Same Drug That You Have Received in This Study For Your Low Back Pain Pain?[52]

End point description:

mPRTI:self-administered questionnaire containing subject reported treatment impact assessment, subject GPA & subject willingness to use drug again assessment. Subjects responded using IRT on 5 point scale from 1-5. Higher scores indicate lesser willingness to use the investigational product. Pre-specified intent of study for efficacy data up to Week 16 was to analyze, subjects who received placebo from Day 1 & received tan 5/10 mg at week 16 in placebo arm, in pooled manner. Data have been reported per four arms. ITT.Pre-specified intent of study was to compare tan Vs placebo for data up to and including week 16 and comparisons of tan Vs tramadol for data up to and including week 56.Number analyzed is 0 for placebo arm for week 16 and onwards. Here "n" =subjects evaluable at specified time point. Data were not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16.

End point type	Secondary

End point timeframe:

Weeks 16 and 56

Notes:

[52] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tanezumab 10 mg	Placebo	Tramadol PR
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	407	407	406	605
Units: subjects				
W16Yes surely want to use SDA(n= 322, 333,340,450)	191	210	167	251
W56Yes surely want to use SDA(n= 0,141,159,206)	99	114	0	133
W16Might want to use SDA(n= 322, 333,340,450)	80	58	61	98
W56Might want to use SDA(n= 0, 141, 159, 206)	23	31	0	41
W16 I am not sure(n= 322, 333,340,450)	36	38	51	64
W56 I am not sure(n= 0, 141, 159, 206)	15	10	0	26
W16:Might not want to use SDA(n= 322, 333,340,450)	10	13	11	13
W56:Might not want to use SDA(n= 0, 141, 159, 206)	0	2	0	4
W16Surely not want to use SDA(n=322,333,340,450)	16	21	32	24
W56Surely not want to use SDA(= 0, 141, 159, 206)	4	2	0	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs) up to End of Study

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs) up to End of Study

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. TE were events between first dose of study drug and up to week 48 that were absent before treatment or that worsened relative to pretreatment state. AEs included both serious and non-serious AEs. Safety population was analyzed. Pre-specified intent of study was for safety summaries until W80 was to summarize data by 4 arms. Hence, number analyzed is 0 for placebo arm for week 16 and onwards. Those who were there up to W16,but switched to tanezumab after W16 are included in tanezumab 5/10 mg arm. Here, "Number of Subjects Analyzed" signifies subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to Week 80

End point values	Placebo	Tanezumab 5 mg Pooled	Tanezumab 10 mg Pooled	Tramadol PR
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	215	506	502	602
Units: subjects				
TEAEs	125	319	347	421
SAEs	7	21	37	25

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Treatment-Related Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects With Treatment-Emergent Treatment-Related Adverse Events (AEs) and Serious Adverse Events (SAEs)[53]

End point description:

Treatment-related AE was any untoward medical occurrence attributed to study drug in a subject who received study drug. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; 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 week 56 that were absent before treatment or that worsened relative to pre-treatment state. Relatedness to study drug was assessed by the investigator.The safety population was defined as all subjects treated with tanezumab or placebo SC. Here, "N"=subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to Week 56

Notes:

[53] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tramadol	Tanezumab 5 mg Pooled	Tanezumab 10 mg Pooled	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	602	506	502	
Units: subjects				
AEs	200	105	119	
SAEs	1	1	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Laboratory Test Abnormalities With Regard to Normal Baseline

End point title	Number of Subjects With Laboratory Test Abnormalities With Regard to Normal Baseline[54]

End point description:

Abnormality criteria:HGB,hematocrit,RBC count <0.8* LLN;Ery. mean corpuscular volume/hemoglobin/ HGB concentration,RBCs distribution width <0.9*LLN, >1.1* ULN; platelets <0.5*LLN, >1.75*ULN;WBC count<0.6*LLN, >1.5*ULN;Lymphocytes, Leukocytes, Neutrophils <0.8*LLN, >1.2*ULN; Basophils,Eosinophils, Monocytes>1.2*ULN;Prothrombin time/Intl. normalized ratio>1.1*ULN;total bilirubin >1.5*ULN; aspartate aminotransferase,alanine aminotransferase,gamma GT,LDH,alkaline phosphatase >3.0*ULN; total protein; albumin<0.8*LLN, >1.2*ULN; blood 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; glucose<0.6*LLN, >1.5*ULN; HGB A1C >1.3*ULN; creatine kinase>2.0*ULN, specific gravity<1.003, >1.030; pH<4.5, >8; Urine Glucose, protein,HGB,bilirubin>=1; Ketones>=1;Urine erythrocytes,Leukocytes>=20.Safety population.“N”=subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to Week 80

Notes:

[54] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tramadol	Placebo	Tanezumab 10 mg Pooled	Tanezumab 5 mg Pooled
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	488	129	433	434
Units: subjects	59	16	61	56

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Laboratory Test Abnormalities With Regard to Abnormal Baseline

End point title	Number of Subjects With Laboratory Test Abnormalities With Regard to Abnormal Baseline[55]

End point description:

Abnormality criteria:hemoglobin;hematocrit; RBC count <0.8*LLN; Ery. mean corpuscular volume/ hemoglobin/ HGB concentration, erythrocytes distribution width <0.9*LLN, >1.1*ULN; platelets <0.5*LLN,>1.75*ULN; white blood cell count<0.6*LLN, >1.5*ULN; Lymphocytes, Leukocytes, Neutrophils <0.8*LLN, >1.2*ULN; Basophils, Eosinophils, Monocytes >1.2*ULN; total bilirubin>1.5*ULN; aspartate aminotransferase, alanine aminotransferase, gamma GT,LDH, alkaline phosphatase >3.0*ULN; total protein; albumin<0.8*LLN, >1.2*ULN; blood 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; glucose <0.6*LLN, >1.5*ULN; Hemoglobin A1C >1.3*ULN; creatine kinase >2.0*ULN; Nitrite >=1.Safety population: all subjects treated with tanezumab or placebo SC. Here “Number of subjects analysed” signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to Week 80

Notes:

[55] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tramadol	Tanezumab 10 mg Pooled	Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	332	373	308	92
Units: subjects	40	45	39	11

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Blood Pressure (BP) at Weeks 2, 4, 8, 16, 24, 32, 40, 48, 56, 64 and 80

End point title	Change From Baseline in Blood Pressure (BP) at Weeks 2, 4, 8, 16, 24, 32, 40, 48, 56, 64 and 80[56]

End point description:

Measurement of BP included sitting systolic blood pressure (SBP) and diastolic blood pressure (DBP). Pre-specified intent of study for safety summaries until W80 was to summarize data by 4 arms. The safety population was defined as all subjects treated with tanezumab or placebo SC. Data not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16. Here, "Number of subjects analyzed"= subjects evaluable for this endpoint and "n"= subjects who were evaluable for specified categories. '99999' = signifies that no subjects were evaluable, hence mean and standard deviation not applicable.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 16, 24, 32, 40, 48, 56, 64 and 80

Notes:

[56] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tramadol	Placebo	Tanezumab 5 mg Pooled	Tanezumab 10 mg Pooled
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	602	215	506	502
Units: millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
SBP: Baseline (n =602, 215, 506, 502)	123.7 (± 13.77)	122.3 (± 12.20)	123.8 (± 13.25)	122.6 (± 12.36)
SBP:Change at Week 2 (n =560, 191, 488, 478)	-1.4 (± 11.37)	-1.3 (± 10.50)	-2.0 (± 11.05)	-1.4 (± 10.62)
SBP:Change at Week 4 (n =535, 173, 473, 468)	-1.8 (± 11.81)	-2.1 (± 11.36)	-2.2 (± 11.46)	-1.7 (± 10.65)
SBP:Change at Week 8 (n =490, 152, 454, 450)	-1.7 (± 11.99)	-1.1 (± 11.37)	-1.0 (± 11.38)	-2.2 (± 11.02)
SBP:Change at Week 16 (n =314, 8, 340, 344)	-1.6 (± 11.96)	-0.5 (± 10.56)	-2.2 (± 10.75)	-1.4 (± 11.10)
SBP:Change at Week 24 (n =269, 0, 288, 295)	-1.9 (± 12.57)	99999 (± 99999)	-2.2 (± 10.51)	-1.8 (± 11.53)

SBP:Change at Week 32 (n =229, 0, 240, 255)	-2.2 (± 12.54)	99999 (± 99999)	-0.6 (± 11.36)	-1.4 (± 11.53)
SBP:Change at Week 40 (n = 218, 0, 218, 239)	-1.0 (± 11.99)	99999 (± 99999)	-2.0 (± 11.27)	-1.6 (± 11.91)
SBP:Change at Week 48 (n = 208, 0, 211, 229)	-0.8 (± 12.46)	99999 (± 99999)	-2.0 (± 12.12)	-2.2 (± 11.51)
SBP:Change at Week 56 (n = 204, 0, 202, 222)	-1.1 (± 12.03)	99999 (± 99999)	-1.5 (± 11.18)	-3.0 (± 12.03)
SBP:Change at Week 64 (n =195, 0, 199, 209)	-1.2 (± 11.59)	99999 (± 99999)	-0.9 (± 11.51)	-1.9 (± 12.28)
SBP:Change at Week 80 (n =191, 0, 193, 201)	-1.0 (± 11.77)	99999 (± 99999)	-1.4 (± 10.82)	0.1 (± 12.62)
DBP: Baseline (n =602, 215, 506, 502)	78.2 (± 9.01)	77.9 (± 9.10)	78.6 (± 8.98)	77.4 (± 8.48)
DBP:Change at Week 2 (n =560, 191, 488, 478)	-0.7 (± 8.21)	-1.2 (± 7.63)	-1.1 (± 7.49)	-1.5 (± 7.91)
DBP:Change at Week 4 (n =535, 173, 473, 468)	-0.9 (± 7.94)	-1.7 (± 7.59)	-1.5 (± 7.75)	-1.1 (± 7.59)
DBP:Change at Week 8 (n =490, 152, 454, 450)	-0.8 (± 8.13)	0.0 (± 7.24)	-1.2 (± 8.04)	-1.5 (± 8.26)
DBP:Change at Week 16 (n =314, 8, 340, 344)	-0.8 (± 8.15)	-0.6 (± 5.63)	-1.2 (± 8.21)	-1.0 (± 8.39)
DBP:Change at Week 24 (n =269, 0, 288, 295)	-1.0 (± 7.76)	99999 (± 99999)	-1.2 (± 8.04)	-0.8 (± 8.13)
DBP:Change at Week 32 (n =229, 0, 240, 255)	-0.4 (± 8.39)	99999 (± 99999)	-0.6 (± 7.80)	-0.5 (± 8.10)
DBP:Change at Week 40 (n = 218, 0, 218, 239)	-0.7 (± 8.36)	99999 (± 99999)	-1.4 (± 8.56)	-1.1 (± 8.13)
DBP:Change at Week 48 (n = 208, 0, 211, 229)	-0.7 (± 7.93)	99999 (± 99999)	-2.1 (± 9.05)	-1.3 (± 8.23)
DBP:Change at Week 56 (n = 204, 0, 202, 222)	-0.7 (± 7.93)	99999 (± 99999)	-2.1 (± 9.05)	-1.3 (± 8.23)
DBP:Change at Week 64 (n =195, 0, 199, 209)	-0.6 (± 8.95)	99999 (± 99999)	-0.7 (± 8.03)	-0.0 (± 9.13)
DBP:Change at Week 80 (n =191, 0, 193, 201)	-0.1 (± 8.55)	99999 (± 99999)	-1.0 (± 8.13)	0.5 (± 9.07)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Heart Rate at Weeks 2, 4, 8, 16, 24, 32, 40, 48, 56, 64 and 80

End point title	Change From Baseline in Heart Rate at Weeks 2, 4, 8, 16, 24, 32, 40, 48, 56, 64 and 80

End point description:

Heart rate was measured at sitting position. Pre-specified intent of study for safety summaries until W80 was to summarize data by 4 arms. The safety population was defined as all subjects treated with tanezumab or placebo SC. Data not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16. Here, "Number of subjects analyzed"= subjects evaluable for this endpoint and "n"= subjects who were evaluable at specified time point for each arm, respectively. '99999' = signifies that no subjects were evaluable, hence mean and standard deviation not applicable.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 16, 24, 32, 40, 48, 56, 64 and 80

End point values	Placebo	Tanezumab 5 mg Pooled	Tanezumab 10 mg Pooled	Tramadol PR
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	215	506	502	602
Units: beats per minute				
arithmetic mean (standard deviation)				
Baseline (n =215, 506, 502, 602)	73.3 (± 10.86)	73.1 (± 10.23)	72.5 (± 10.10)	73.2 (± 10.61)
Change at Week 2 (n =191, 488, 478, 560)	0.8 (± 9.14)	0.5 (± 9.09)	0.3 (± 9.23)	-0.2 (± 9.24)
Change at Week 4 (n =173, 473, 468, 535)	1.6 (± 9.32)	0.6 (± 8.82)	0.4 (± 9.47)	0.2 (± 9.57)
Change at Week 8 (n =152, 454, 450, 490)	1.2 (± 8.88)	0.1 (± 9.41)	-0.1 (± 9.87)	0.0 (± 9.89)
Change at Week 16 (n =8, 340, 344, 314)	5.1 (± 10.66)	-0.6 (± 9.99)	-1.0 (± 9.65)	-0.8 (± 10.13)
Change at Week 24 (n =0, 288, 295, 269)	99999 (± 99999)	0.0 (± 9.32)	-0.3 (± 9.77)	0.2 (± 10.09)
Change at Week 32 (n =0, 240, 255, 229)	99999 (± 99999)	0.5 (± 9.82)	-0.3 (± 9.94)	0.6 (± 9.72)
Change at Week 40 (n =0, 218, 239, 218)	99999 (± 99999)	1.2 (± 10.14)	-0.5 (± 9.77)	1.3 (± 9.55)
Change at Week 48 (n =0, 211, 229, 208)	99999 (± 99999)	0.5 (± 9.72)	-0.5 (± 10.79)	0.9 (± 10.33)
Change at Week 56 (n =0, 202, 222, 204)	99999 (± 99999)	0.4 (± 10.31)	0.2 (± 10.50)	0.7 (± 11.10)
Change at Week 64 (n =0, 199, 209, 195)	99999 (± 99999)	1.1 (± 10.66)	0.8 (± 10.08)	0.7 (± 10.22)
Change at Week 80 (n =0, 193, 201, 191)	99999 (± 99999)	1.1 (± 10.93)	1.2 (± 9.83)	0.9 (± 11.48)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Electrocardiogram (ECG) Parameters at Weeks 16, 56 and 80

End point title	Change From Baseline in Electrocardiogram (ECG) Parameters at Weeks 16, 56 and 80[57]

End point description:

A 12–lead ECG was recorded after subjects had rested for at least 5 minutes in the supine position in a quiet environment. All standard intervals {RR interval, PR interval, QRS interval, QT interval, QT interval corrected using Bazett's formula (QTcB) and QT interval corrected using Fridericia's formula (QTcF)} were collected. Pre-specified intent of study for safety summaries until W80 was to summarize data by 4 arms. The safety population was defined as all subjects treated with tanezumab or placebo SC. Data not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16. Here, 'Number of subjects analyzed' signifies subjects analyzed for this endpoint and 'n' = subjects who had at least 1 ADA sample for ADA assessment at specified time points. '99999' = signifies that no subjects were evaluable, hence mean and standard deviation not applicable.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 56 and 80

Notes:

[57] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis was planned for this endpoint

End point values	Tramadol	Placebo	Tanezumab 5 mg Pooled	Tanezumab 10 mg Pooled
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	602	215	506	502
Units: millisecond				
arithmetic mean (standard deviation)				
RR Interval: Baseline (n= 602, 215, 506, 502)	918.9 (± 138.55)	928.5 (± 150.40)	911.4 (± 140.72)	915.4 (± 138.41)
RR Interval:Change at Week 16(n= 308, 6, 338, 335)	894.9 (± 139.62)	868.2 (± 235.72)	897.1 (± 129.55)	912.1 (± 142.81)
RR Interval:Change at Week 56(n= 202, 0, 200, 221)	881.5 (± 136.11)	99999 (± 99999)	894.5 (± 138.03)	893.0 (± 144.30)
RR Interval:Change at Week 80(n= 190, 0, 190, 199)	876.5 (± 134.79)	99999 (± 99999)	870.5 (± 130.84)	889.6 (± 143.10)
PR Interval: Baseline(n= 596, 213, 506, 501)	157.8 (± 23.44)	156.2 (± 20.51)	157.3 (± 23.32)	158.1 (± 22.93)
PR Interval:CAW 16(n= 308, 6, 337, 334)	158.6 (± 23.37)	158.8 (± 12.37)	158.3 (± 21.99)	159.6 (± 21.84)
PR Interval:CAW 56(n= 202, 0, 199, 221)	159.2 (± 22.13)	99999 (± 99999)	158.5 (± 21.78)	158.1 (± 20.85)
PR Interval:CAW 80(n= 189, 0, 190, 198)	158.3 (± 21.46)	99999 (± 99999)	158.7 (± 22.15)	157.7 (± 21.60)
QRS Interval: Baseline(n= 599, 215, 506, 502)	93.1 (± 12.02)	90.9 (± 8.72)	92.5 (± 11.06)	93.5 (± 12.30)
QRS Interval:CAW 16(n= 308,6,338, 335)	93.9 (± 12.53)	97.0 (± 8.29)	93.4 (± 11.95)	94.5 (± 13.27)
QRS Interval:CAW 56(n= 202, 0, 200, 221)	94.2 (± 13.73)	99999 (± 99999)	92.8 (± 12.71)	95.4 (± 12.62)
QRS Interval:CAW 80(n= 190,0,190,199)	94.4 (± 13.16)	99999 (± 99999)	93.0 (± 11.55)	95.0 (± 12.53)
QT Interval:Baseline(n=599,215,504, 502)	393.7 (± 29.06)	394.7 (± 29.67)	393.1 (± 29.52)	394.6 (± 27.54)
QT Interval:CAW 16(n=308,6,337,334)	391.2 (± 30.30)	379.8 (± 34.29)	391.1 (± 28.13)	393.5 (± 29.09)
QT Interval:CAW 56(n=201,0,200,221)	389.7 (± 29.44)	99999 (± 99999)	389.3 (± 27.11)	392.8 (± 29.47)
QT Interval:CAW 80(n=190, 0, 190, 198)	388.7 (± 29.33)	99999 (± 99999)	386.6 (± 27.67)	393.0 (± 29.90)
QTCB Interval:Baseline(n=599,215,504, 502)	412.6 (± 22.39)	411.7 (± 20.49)	413.5 (± 20.19)	414.4 (± 21.60)
QTCB Interval:CAW 16(n=308,6,337,334)	415.3 (± 20.13)	411.8 (± 17.50)	414.5 (± 19.76)	413.9 (± 22.67)
QTCB Interval:CAW 56(n=201,0,200,221)	416.8 (± 21.71)	99999 (± 99999)	413.5 (± 21.27)	417.7 (± 22.02)
QTCB Interval:CAW 80(n=190,0,190,198)	417.0 (± 21.71)	99999 (± 99999)	416.1 (± 19.27)	418.8 (± 22.13)
QTCF Interval:Baseline(n=599,215,504,502)	405.9 (± 20.28)	405.6 (± 18.22)	406.3 (± 18.85)	407.4 (± 18.93)
QTCF Interval:CAW16(n=308,6,337,334)	406.8 (± 19.04)	400.3 (± 10.69)	406.3 (± 18.45)	406.7 (± 20.35)
QTCF Interval:CAW 56(n=201,0,200,221)	407.3 (± 19.74)	99999 (± 99999)	405.0 (± 18.46)	408.9 (± 19.75)
QTCF Interval:CAW 80(n=190,0,190,198)	407.1 (± 19.81)	99999 (± 99999)	405.7 (± 17.70)	409.7 (± 19.74)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Heart Rate (as assessed by ECG) at Weeks 16, 56 and 80

End point title	Change From Baseline in Heart Rate (as assessed by ECG) at Weeks 16, 56 and 80

End point description:

Heart rate was measured at sitting position. Pre-specified intent of study for safety summaries until W80 was to summarize data by 4 arms. The safety population was defined as all subjects treated with tanezumab or placebo SC. Data not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16. Here, 'Number of subjects analyzed' signifies subjects analyzed for this endpoint and 'n' = subjects who had at least 1 ADA sample for ADA assessment at specified time points. '99999' = signifies that no subjects were evaluable, hence mean and standard deviation not applicable.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 56 and 80

End point values	Placebo	Tanezumab 5 mg Pooled	Tanezumab 10 mg Pooled	Tramadol PR
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	215	506	502	602
Units: beats per minute				
arithmetic mean (standard deviation)				
Baseline (n =215, 506, 502, 599)	66.4 (± 11.34)	67.4 (± 10.34)	67.1 (± 10.31)	66.9 (± 10.64)
Change at Week 16 (n =6, 338, 335, 308)	72.3 (± 14.42)	68.3 (± 10.00)	67.4 (± 10.35)	68.8 (± 10.99)
Change at Week 56 (n =0, 200, 221, 202)	99999 (± 99999)	68.6 (± 10.29)	68.9 (± 11.02)	69.7 (± 11.26)
Change at Week 80 (n =0, 190, 199, 190)	99999 (± 99999)	70.5 (± 10.57)	69.3 (± 11.61)	70.1 (± 10.98)

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[58]

End point description:

Orthostatic hypotension was defined as postural change (supine to standing) that met the following criteria: For SBP <=150 mmHg: Reduction in SBP >=20 mmHg or reduction in DBP >=10 mmHg at the 1 and/or 3 minute standing BP measurements. Pre-specified intent of study for safety summaries until

W80 was to summarize data by 4 arms. Data not collected after W16 in placebo arm for this endpoint, as those who met criteria to continue, switched to active treatment with tanezumab after W16. The safety population was defined as all subjects treated with tanezumab or placebo SC. Here, 'Number of subjects analyzed' signifies subjects analyzed for this endpoint and 'n' = subjects who had at least 1 ADA sample for ADA assessment at specified time points. 'N' in placebo arm=subjects who received only placebo for entire study, those who were there up to W16,but switched to tanezumab after W16 are included in tanezumab 5/10mg arm. '99999' = signifies that no subjects were evaluable.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 16, 24, 32, 40, 48, 56, 64 and 80

Notes:

[58] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tramadol	Placebo	Tanezumab 5 mg Pooled	Tanezumab 10 mg Pooled
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	601	215	503	501
Units: subjects				
Baseline (n =601, 215, 503, 501)	2	0	1	0
Week 2 (n =552, 186, 482, 477)	0	1	0	0
Week 4 (n =527, 171, 473, 465)	2	0	2	0
Week 8 (n =485, 151, 452, 445)	1	0	0	0
Week 16 (n =321, 21, 339, 352)	0	0	1	1
Week 24 (n =266, 0, 286, 297)	0	0	0	0
Week 32 (n =228, 0, 241, 255)	0	0	0	0
Week 40 (n =218, 0, 218, 236)	1	0	0	0
Week 48 (n =208, 0, 211, 227)	0	0	1	0
Week 56 (n =204, 0, 202, 223)	0	0	0	1
Week 64 (n =194, 0, 198, 209)	0	0	1	0
Week 80 (n =192, 0, 200, 191)	0	0	1	1

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Screening in Survey of Autonomic Symptom (SAS) Scores at Weeks 24, 56 and 80

End point title	Change From Screening in Survey of Autonomic Symptom (SAS) Scores at Weeks 24, 56 and 80[59]

End point description:

SAS is a 12 item (11 for females) questionnaire, from which the total number of symptoms (0-12 for males and 0-11 for females) is calculated. Each positive symptom is rated from 1 (not at all) to 5 (a lot). Total impact score was sum of all symptom rating scores, with 0 assigned where the subject did not have the particular symptom. Range for total impact score is 0-60 for males and 0-55 for females, where higher scores indicating higher impact. Pre-specified intent of study for safety summaries until W80 was to summarize data by 4 arms. The safety population was defined as all subjects treated with tanezumab or placebo SC. Data not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16.'n' = subjects who had at least 1 ADA sample for ADA assessment at specified time points. '99999' =no subjects were evaluable, hence mean and SD not applicable. # signifies number and TSIS signifies Total Symptom Impact Score.

End point type	Secondary

End point timeframe:

Screening (up to maximum of 37 days prior to Baseline), Weeks 24, 56 and 80

Notes:

[59] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tramadol	Placebo	Tanezumab 5 mg Pooled	Tanezumab 10 mg Pooled
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	602	215	506	502
Units: units on a scale				
arithmetic mean (standard deviation)				
# of symptom reported:Screening(n=602,215,506,502	0.48 (± 0.74)	0.45 (± 0.79)	0.43 (± 0.75)	0.50 (± 0.82)
# of symptoms reported:CAW 24 (n= 268,0,287,295)	0.51 (± 1.34)	99999 (± 99999)	0.32 (± 1.45)	0.28 (± 1.37)
# of symptoms reported: CAW 56(n=204,0,202,223)	0.60 (± 1.49)	99999 (± 99999)	0.50 (± 1.57)	0.30 (± 1.37)
# of symptoms reported:CAW 80(n=191,0,193,201)	0.45 (± 1.47)	99999 (± 99999)	0.41 (± 1.38)	0.42 (± 1.45)
TSIS :Screening (n=602,215,506,502)	1.06 (± 1.71)	0.93 (± 1.62)	0.95 (± 1.69)	1.10 (± 1.88)
TSIS: CAW 24 (n= 268, 0, 287, 295)	1.37 (± 3.68)	99999 (± 99999)	1.03 (± 4.05)	0.76 (± 3.55)
TSIS: CAW 56 (n= 204, 0, 202, 223)	1.74 (± 3.96)	99999 (± 99999)	1.49 (± 4.53)	0.96 (± 3.87)
TSIS: CAW 80 (n= 191, 0, 193, 201)	1.43 (± 3.94)	99999 (± 99999)	1.47 (± 4.26)	1.28 (± 4.10)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Adjudicated Joint Safety Outcomes

End point title	Percentage of Subjects With Adjudicated Joint Safety

End point description:

Incidence of subjects with any of the joint safety adjudication outcomes of primary osteonecrosis, rapidly progressive OA (type 1 and type 2), subchondral insufficiency fracture (or SPONK), or pathological fracture. The safety population was defined as all subjects treated with tanezumab or placebo SC. Pre-specified intent of study for safety summaries until W80 was to summarize data by 4 arms. 'N' in placebo arm=subjects who received only placebo for entire study, those who were there up to W16,but switched to tanezumab after W16 are included in tanezumab 5/10mg arm.

End point type	Secondary

End point timeframe:

Baseline up to Week 80

Notes:

[60] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tramadol	Placebo	Tanezumab 5 mg Pooled	Tanezumab 10 mg Pooled
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	602	215	506	502
Units: percentage of subjects				
number (confidence interval 95%)				
Composite Joint Safety Endpoint	0.2 (0.0 to 0.9)	0 (0.0 to 1.7)	1.0 (0.3 to 2.3)	2.6 (1.4 to 4.4)
Rapidly Progressive OA	0.2 (0.0 to 0.9)	0 (0.0 to 1.7)	1.0 (0.3 to 2.3)	1.8 (0.8 to 3.4)
Rapidly Progressive OA type 1	0.2 (0.0 to 0.9)	0 (0.0 to 1.7)	1.0 (0.3 to 2.3)	1.4 (0.6 to 2.9)
Rapidly Progressive OA type 2	0 (0.0 to 0.6)	0 (0.0 to 1.7)	0 (0.0 to 0.7)	0.4 (0.0 to 1.4)
Primary Osteonecrosis	0 (0.0 to 0.6)	0 (0.0 to 1.7)	0 (0.0 to 0.7)	0 (0.0 to 0.7)
Pathological Fracture	0 (0.0 to 0.6)	0 (0.0 to 1.7)	0 (0.0 to 0.7)	0 (0.0 to 0.7)
Subchondral Insufficiency Fracture	0 (0.0 to 0.6)	0 (0.0 to 1.7)	0 (0.0 to 0.7)	0.8 (0.2 to 2.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Total Joint Replacements

End point title	Percentage of Subjects With Total Joint Replacements[61]

End point description:

Percentage of subjects who underwent at least one total knee, hip or shoulder joint replacement surgery. The safety population was defined as all subjects treated with tanezumab or placebo SC. Pre-specified intent of study for safety summaries until W80 was to summarize data by 4 arms. N in placebo arm=number of subjects who received only placebo for entire study, those who were there up to W16,but switched to tanezumab treatment after W16 are included in tanezumab 5/10 mg arm.

End point type	Secondary

End point timeframe:

Baseline up to Week 80

Notes:

[61] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tramadol	Placebo	Tanezumab 5 mg Pooled	Tanezumab 10 mg Pooled
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	602	215	506	502
Units: percentage of subjects				
number (confidence interval 95%)	0 (0.0 to 0.6)	0 (0.0 to 1.7)	0 (0.0 to 0.7)	1.4 (0.6 to 2.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Neuropathy Impairment Score (NIS) at Weeks 2, 4, 8, 16, 24, 32, 40, 48, 56, 64 and 80

End point title	Change From Baseline in Neuropathy Impairment Score (NIS)

	at Weeks 2, 4, 8, 16, 24, 32, 40, 48, 56, 64 and 80[62]

End point description:

NIS is standardized instrument used to evaluate subject for signs of peripheral neuropathy. NIS is sum of scores of 37 items, from both the left and right side, where 24 items scored from 0 (normal) to 4 (paralysis), higher score indicated higher abnormality/impairment and 13 items scored from 0 (normal), 1 (decreased) and 2 (absent), higher score indicated higher impairment. NIS possible overall score ranged from 0 (no impairment) to 244(maximum impairment), higher scores indicated increased impairment. Pre-specified intent of study for safety summaries until W80 was to summarize data by 4 arms. The safety population was defined as all subjects treated with tanezumab or placebo SC. Data not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16. Here, 'n' = subjects who had at least 1 ADA sample for ADA assessment at specified time points. '99999' =no subjects were evaluable, hence mean and SD not applicable.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 16, 24, 32, 40, 48, 56, 64 and 80

Notes:

[62] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tramadol	Placebo	Tanezumab 5 mg Pooled	Tanezumab 10 mg Pooled
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	602	215	506	502
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n =601, 215, 506, 502)	0.78 (± 2.62)	1.00 (± 3.55)	0.58 (± 2.28)	0.86 (± 2.54)
Change at Week 2 (n =565, 190, 488, 475)	-0.15 (± 1.31)	0.02 (± 1.29)	0.05 (± 1.12)	-0.08 (± 1.34)
Change at Week 4 (n =579, 198, 492, 487)	-0.16 (± 1.36)	-0.14 (± 1.35)	-0.02 (± 0.96)	-0.17 (± 1.57)
Change at Week 8 (n =590, 200, 495, 490)	0.08 (± 3.53)	0.01 (± 1.97)	-0.09 (± 1.41)	-0.17 (± 1.99)
Change at Week 16 (n =590, 200, 495, 490)	0.02 (± 1.84)	-0.02 (± 1.91)	-0.06 (± 1.37)	-0.06 (± 1.94)
Change at Week 24 (n =590, 0, 495, 491)	0.03 (± 2.32)	99999 (± 99999)	-0.10 (± 1.58)	-0.09 (± 1.77)
Change at Week 32 (n =590, 0, 495, 491)	0.03 (± 1.90)	99999 (± 99999)	-0.14 (± 1.60)	-0.12 (± 1.73)
Change at Week 40 (n =590, 0, 495, 491)	-0.02 (± 1.97)	99999 (± 99999)	-0.13 (± 1.44)	-0.13 (± 1.81)
Change at Week 48 (n =590, 0, 495, 491)	0.00 (± 1.92)	99999 (± 99999)	-0.14 (± 1.33)	-0.10 (± 1.85)
Change at Week 56 (n =590, 0, 495, 491)	-0.03 (± 1.97)	99999 (± 99999)	-0.16 (± 1.38)	-0.09 (± 2.07)
Change at Week 64 (n =590, 0, 495, 491)	-0.06 (± 2.03)	99999 (± 99999)	-0.07 (± 2.39)	-0.09 (± 2.06)
Change at Week 80 (n =590, 0, 495, 491)	-0.07 (± 2.06)	99999 (± 99999)	-0.09 (± 1.94)	-0.12 (± 2.15)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Anti Tanezumab Antibodies

End point title	Number of Subjects With Anti Tanezumab Antibodies[63]

End point description:

Human serum anti-drug antibody (ADA) samples were analyzed for the presence or absence of anti-tanezumab antibodies by using a semi quantitative enzyme linked immunosorbent assay (ELISA). Subjects listed as having anti-tanezumab antibodies had ADA titer level >=3.32. Less than 3.32 was considered below the limit of quantitation. Pre-specified intent of study for safety summaries until W80 was to summarize data by 4 arms. The safety population was defined as all subjects treated with tanezumab or placebo SC. Here, 'n' = subjects who had at least 1 ADA sample for ADA assessment at specified time points. Data not collected after W16 in placebo arm, as those who met criteria to continue, switched to active treatment with tanezumab after W16. '99999' = signifies that no subjects were evaluable.

End point type	Secondary

End point timeframe:

Baseline, Weeks 8, 16, 32, 40, 48, 56, 64 and 80

Notes:

[63] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint

End point values	Tanezumab 5 mg	Tramadol	Pooled Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	407	407	409	
Units: subjects				
Baseline (n =402, 404, 402)	38	39	45	
Week 8 (n = 402, 341, 347)	32	54	37	
Week 16 (n =241, 200, 235)	36	46	27	
Week 32 (n =166, 181, 0)	32	48	99999	
Week 40 (n =0, 0, 0)	99999	99999	99999	
Week 48 (n =145, 160, 0)	31	49	99999	
Week 56 (n =138, 157, 0)	22	41	99999	
Week 64 (n =135, 146, 0)	15	32	99999	
Week 80 (n =131, 143, 0)	14	14	99999	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 80

Adverse event reporting additional description:

Same event may appear as both an AE and SAE. Event may be categorized as serious in 1 subject and as NS in another, or a subject may have experienced both a SAE and NSAE. N in placebo arm = subjects who received only placebo for entire study, those who were there up to W16,but switched to tanezumab after W16 included in tanezumab 5/10mg arm.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Tanezumab 5 mg

Reporting group description:

Tanezumab (RN624 or PF-04383119) 5 mg injection administered SC once every 8 weeks from Day 1 and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 56.

Reporting group title	Tanezumab 10 mg

Reporting group description:

Tanezumab (RN624 or PF-04383119) 10 mg injection administered SC once every 8 weeks from Day 1, and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 56.

Reporting group title	Tramadol

Reporting group description:

Tramadol PR tablet of 100 mg (during baseline to week 4, dose increments by 100 mg was allowed up to a maximum of 300 mg, depending on pain relief or tolerability), once daily and placebo injection matched to tramadol, administered SC once every 8 weeks, from Day 1 up to week 56.

Reporting group title	Placebo

Reporting group description:

Placebo matched to tanezumab (RN624 or PF-04383119) injection administered SC, once every 8 weeks from Day 1 (baseline), and placebo tablets matched to tramadol PR, orally, once daily from Day 1 up to week 56.

Serious adverse events	Tanezumab 5 mg	Tanezumab 10 mg	Tramadol
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 506 (4.15%)	37 / 502 (7.37%)	25 / 602 (4.15%)
number of deaths (all causes)	4	2	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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 malignant			

subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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
Prostate cancer			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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
Rectal cancer			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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
Small cell lung cancer			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	0 / 602 (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			
Aneurysm			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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
Aneurysm ruptured			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic aneurysm			

subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	0 / 602 (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
Pregnancy, puerperium and perinatal conditions			
Foetal death			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Unintended pregnancy			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 506 (0.20%)	1 / 502 (0.20%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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
Reproductive system and breast disorders			
Prostatitis			

subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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			
Acute respiratory failure			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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
Pneumonia aspiration			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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
Pulmonary hypertension			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Major depression			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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
Depression suicidal			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	0 / 602 (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			
Ankle fracture			
subjects affected / exposed	1 / 506 (0.20%)	1 / 502 (0.20%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament sprain			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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
Limb injury			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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
Meniscus injury			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural nausea			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Road traffic accident			
subjects affected / exposed	0 / 506 (0.00%)	2 / 502 (0.40%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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
Toxicity to various agents			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Urinary retention postoperative			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	0 / 602 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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 failure			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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
Coronary artery disease			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			

subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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
Palpitations			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Guillain-Barre syndrome			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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
Lumbar radiculopathy			
subjects affected / exposed	0 / 506 (0.00%)	2 / 502 (0.40%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			

subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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 / 506 (0.00%)	0 / 502 (0.00%)	2 / 602 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deafness neurosensory			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	0 / 602 (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
Eye disorders			
Pupils unequal			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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
Uveitis			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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
Anal fistula			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Colitis ischaemic			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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
Large intestine perforation			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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
Oesophageal rupture			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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			
Biliary dyskinesia			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			

subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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
Nephrolithiasis			
subjects affected / exposed	1 / 506 (0.20%)	1 / 502 (0.20%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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
Urinary incontinence			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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
Intervertebral disc compression			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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
Intervertebral disc protrusion			
subjects affected / exposed	1 / 506 (0.20%)	1 / 502 (0.20%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Muscular weakness			
subjects affected / exposed	1 / 506 (0.20%)	1 / 502 (0.20%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 506 (0.00%)	3 / 502 (0.60%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rapidly progressive osteoarthritis			
subjects affected / exposed	0 / 506 (0.00%)	5 / 502 (1.00%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 506 (0.00%)	3 / 502 (0.60%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subchondral insufficiency fracture			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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
Amoebic colitis			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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
Arthritis infective			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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
Influenza			

subjects affected / exposed	1 / 506 (0.20%)	1 / 502 (0.20%)	0 / 602 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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
Sepsis			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 506 (0.00%)	0 / 502 (0.00%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	1 / 506 (0.20%)	0 / 502 (0.00%)	0 / 602 (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
Tooth abscess			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	0 / 602 (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
Urinary tract infection			
subjects affected / exposed	0 / 506 (0.00%)	1 / 502 (0.20%)	1 / 602 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 215 (3.26%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neoplasm malignant			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal cancer			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small cell lung cancer			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung adenocarcinoma			
subjects affected / exposed	1 / 215 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Aneurysm			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aneurysm ruptured			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Deep vein thrombosis			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aortic aneurysm			
subjects affected / exposed	1 / 215 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Foetal death			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Unintended pregnancy			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypersensitivity			

subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary hypertension			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			

subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Major depression			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mental status changes			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Depression suicidal			
subjects affected / exposed	1 / 215 (0.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ligament sprain			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Limb injury			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Meniscus injury				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Procedural nausea				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				
subjects affected / exposed	1 / 215 (0.47%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toxicity to various agents				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary retention postoperative				
subjects affected / exposed	1 / 215 (0.47%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial fibrillation				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	1 / 215 (0.47%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac failure congestive				

subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Palpitations				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Carpal tunnel syndrome				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Guillain-Barre syndrome				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lumbar radiculopathy				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				

subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	0 / 215 (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	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Deafness neurosensory			
subjects affected / exposed	1 / 215 (0.47%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Pupils unequal			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uveitis			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Anal fistula			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis ischaemic			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hiatus hernia			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Large intestine perforation			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oesophageal rupture			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			

Biliary dyskinesia			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ureterolithiasis			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary incontinence			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Intervertebral disc compression				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc protrusion				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rapidly progressive osteoarthritis				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rotator cuff syndrome				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subchondral insufficiency fracture				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abdominal abscess				
subjects affected / exposed	0 / 215 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Amoebic colitis				

subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arthritis infective			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal sepsis			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tooth abscess			
subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			

subjects affected / exposed	0 / 215 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Tanezumab 5 mg	Tanezumab 10 mg	Tramadol
Total subjects affected by non-serious adverse events			
subjects affected / exposed	201 / 506 (39.72%)	203 / 502 (40.44%)	275 / 602 (45.68%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	26 / 506 (5.14%)	20 / 502 (3.98%)	18 / 602 (2.99%)
occurrences (all)	31	22	20
Nervous system disorders			
Dizziness			
subjects affected / exposed	12 / 506 (2.37%)	11 / 502 (2.19%)	44 / 602 (7.31%)
occurrences (all)	12	12	47
Headache			
subjects affected / exposed	39 / 506 (7.71%)	36 / 502 (7.17%)	50 / 602 (8.31%)
occurrences (all)	48	39	62
Somnolence			
subjects affected / exposed	5 / 506 (0.99%)	7 / 502 (1.39%)	33 / 602 (5.48%)
occurrences (all)	5	7	36
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	9 / 506 (1.78%)	12 / 502 (2.39%)	52 / 602 (8.64%)
occurrences (all)	10	13	53
Nausea			
subjects affected / exposed	16 / 506 (3.16%)	16 / 502 (3.19%)	78 / 602 (12.96%)
occurrences (all)	21	17	82
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	68 / 506 (13.44%)	71 / 502 (14.14%)	65 / 602 (10.80%)
occurrences (all)	87	97	83
Back pain			

subjects affected / exposed	39 / 506 (7.71%)	33 / 502 (6.57%)	33 / 602 (5.48%)
occurrences (all)	49	36	40
Musculoskeletal pain			
subjects affected / exposed	36 / 506 (7.11%)	27 / 502 (5.38%)	31 / 602 (5.15%)
occurrences (all)	37	33	36
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	31 / 506 (6.13%)	32 / 502 (6.37%)	37 / 602 (6.15%)
occurrences (all)	34	39	42
Upper respiratory tract infection			
subjects affected / exposed	25 / 506 (4.94%)	34 / 502 (6.77%)	30 / 602 (4.98%)
occurrences (all)	28	37	35

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	65 / 215 (30.23%)		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	4 / 215 (1.86%)		
occurrences (all)	4		
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 215 (1.86%)		
occurrences (all)	4		
Headache			
subjects affected / exposed	13 / 215 (6.05%)		
occurrences (all)	20		
Somnolence			
subjects affected / exposed	6 / 215 (2.79%)		
occurrences (all)	6		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	3 / 215 (1.40%)		
occurrences (all)	3		
Nausea			
subjects affected / exposed	5 / 215 (2.33%)		
occurrences (all)	5		

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	22 / 215 (10.23%)		
occurrences (all)	39		
Back pain			
subjects affected / exposed	15 / 215 (6.98%)		
occurrences (all)	16		
Musculoskeletal pain			
subjects affected / exposed	12 / 215 (5.58%)		
occurrences (all)	12		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	11 / 215 (5.12%)		
occurrences (all)	12		
Upper respiratory tract infection			
subjects affected / exposed	4 / 215 (1.86%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 July 2015	Clarification to the prohibited medications in Section 5.8.1 and Appendix 4, to specify that opioids analgesics are prohibited through Week 64.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported