Clinical trial results:
A Phase 3, Multicenter, Long-Term Observational Study of Subjects From Tanezumab Studies who Undergo a Total Knee, Hip or Shoulder Replacement

Summary

EudraCT number	2013-002549-12
Trial protocol	HU AT ES BG DE PT FI GB SE LT HR
Global end of trial date	15 July 2019

Results information

Result version number	v1 (current)
This version publication date	23 July 2020
First version publication date	23 July 2020

Trial information

Trial identification

Sponsor protocol code	A4091064

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02674386
WHO universal trial number (UTN)	-
Other trial identifiers	TJR FOLLOW-UP: TJR FOLLOW-UP

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 1-800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 1-800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 October 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the post-operative outcome of subjects who underwent a total knee, hip, or shoulder replacement while participating in tanezumab Study A4091056, A4091057 or A4091058 (treatment period and safety follow-up period).

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 Harmonisation (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	23 August 2016
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	Australia: 1
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Hungary: 32
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Japan: 8
Country: Number of subjects enrolled	Lithuania: 4
Country: Number of subjects enrolled	New Zealand: 6
Country: Number of subjects enrolled	Portugal: 1
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	Serbia: 1
Country: Number of subjects enrolled	Slovakia: 2
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Sweden: 5
Country: Number of subjects enrolled	United States: 80
Worldwide total number of subjects	150
EEA total number of subjects	48

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)	73
From 65 to 84 years	75
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Included subjects from studies A4091056 (NCT02697773), A4091057 (NCT02709486) and A4091058 (NCT02528188) who had undergone a total joint replacement (TJR) surgery of knee, hip, or shoulder. If subject underwent an additional TJR surgery, data for that was also assessed.154 subjects were enrolled out of which only 150 met study eligibility criteria.

Pre-assignment

Screening details:

Pre-specified intent of this study was to compare results regardless of treatment group/doses in parent studies and also to report data for overall (combined subjects from all parent studies).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects who received placebo matched to tanezumab in studies A4091056 (NCT02697773) and A4091057 (NCT02709486) and who had undergone a TJR surgery, were followed up for a maximum duration of 24 weeks in this study. Baseline for this study was the last visit in study A4091056, A4091057 or A4091058 (NCT02528188) or when the site notified of a planned TJR surgery.

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

Dosage and administration details:

Placebo matched to tanezumab in studies A4091056 (NCT02697773) and A4091057 (NCT02709486).

Arm title	Tanezumab Combined

Arm description:

Subjects who received tanezumab subcutaneous (SC) injection of 2.5 milligram (mg) or 2.5 mg/5 mg or 5 mg in studies A4091056, A4091057 or A4091058 and who had undergone a TJR surgery, were followed up for a maximum duration of 24 weeks in this study. Baseline for this study was the last visit in study A4091056, A4091057 or A4091058 or when the site notified of a planned TJR surgery.

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

Dosage and administration details:

Tanezumab SC injection of 2.5 mg or 2.5 mg/5 mg or 5 mg in studies A4091056, A4091057 or A4091058.

Arm title	NSAID

Arm description:

Subjects who received non-steroidal anti-inflammatory drug (NSAID) tablets (naproxen 500 mg, celecoxib 100 mg, or diclofenac extended release 75 mg) in study A4091058 and who had undergone a

TJR surgery, were followed up for a maximum duration of 24 weeks in this study. Baseline for this study was the last visit in study A4091056, A4091057 or A4091058 or when the site notified of a planned TJR surgery.

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

Dosage and administration details:

NSAID tablets (naproxen 500 mg, celecoxib 100 mg, or diclofenac extended release 75 mg) in study A4091058.

Number of subjects in period 1	Placebo	Tanezumab Combined	NSAID
Started	20	113	17
Completed	20	107	16
Not completed	0	6	1
Consent withdrawn by subject	-	4	-
Unspecified	-	1	-
Lost to follow-up	-	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects who received placebo matched to tanezumab in studies A4091056 (NCT02697773) and A4091057 (NCT02709486) and who had undergone a TJR surgery, were followed up for a maximum duration of 24 weeks in this study. Baseline for this study was the last visit in study A4091056, A4091057 or A4091058 (NCT02528188) or when the site notified of a planned TJR surgery.	
Reporting group title	Tanezumab Combined
Reporting group description:	
Subjects who received tanezumab subcutaneous (SC) injection of 2.5 milligram (mg) or 2.5 mg/5 mg or 5 mg in studies A4091056, A4091057 or A4091058 and who had undergone a TJR surgery, were followed up for a maximum duration of 24 weeks in this study. Baseline for this study was the last visit in study A4091056, A4091057 or A4091058 or when the site notified of a planned TJR surgery.	
Reporting group title	NSAID
Reporting group description:	
Subjects who received non-steroidal anti-inflammatory drug (NSAID) tablets (naproxen 500 mg, celecoxib 100 mg, or diclofenac extended release 75 mg) in study A4091058 and who had undergone a TJR surgery, were followed up for a maximum duration of 24 weeks in this study. Baseline for this study was the last visit in study A4091056, A4091057 or A4091058 or when the site notified of a planned TJR surgery.	

Reporting group values	Placebo	Tanezumab Combined	NSAID
Number of subjects	20	113	17
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)	9	55	9
From 65-84 years	10	57	8
85 years and over	0	0	0
Unspecified	1	1	0
Age Continuous			
Units: Years			
arithmetic mean	65.26	64.57	62.94
standard deviation	± 8.77	± 8.18	± 9.13
Sex/Gender, Customized			
Units: Subjects			
Male	6	50	4
Female	13	62	13
Unspecified	1	1	0
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	6	0

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	6	3
White	17	100	14
More than one race	0	0	0
Unknown or Not Reported	1	1	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	3	3
Not Hispanic or Latino	18	109	14
Unknown or Not Reported	1	1	0

Reporting group values	Total		
Number of subjects	150		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	73		
From 65-84 years	75		
85 years and over	0		
Unspecified	2		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	-		
Sex/Gender, Customized			
Units: Subjects			
Male	60		
Female	88		
Unspecified	2		
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	8		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	9		
White	131		
More than one race	0		
Unknown or Not Reported	2		
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	7		
Not Hispanic or Latino	141		
Unknown or Not Reported	2		

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects who received placebo matched to tanezumab in studies A4091056 (NCT02697773) and A4091057 (NCT02709486) and who had undergone a TJR surgery, were followed up for a maximum duration of 24 weeks in this study. Baseline for this study was the last visit in study A4091056, A4091057 or A4091058 (NCT02528188) or when the site notified of a planned TJR surgery.

Reporting group title	Tanezumab Combined

Reporting group description:

Subjects who received tanezumab subcutaneous (SC) injection of 2.5 milligram (mg) or 2.5 mg/5 mg or 5 mg in studies A4091056, A4091057 or A4091058 and who had undergone a TJR surgery, were followed up for a maximum duration of 24 weeks in this study. Baseline for this study was the last visit in study A4091056, A4091057 or A4091058 or when the site notified of a planned TJR surgery.

Reporting group title	NSAID

Reporting group description:

Subjects who received non-steroidal anti-inflammatory drug (NSAID) tablets (naproxen 500 mg, celecoxib 100 mg, or diclofenac extended release 75 mg) in study A4091058 and who had undergone a TJR surgery, were followed up for a maximum duration of 24 weeks in this study. Baseline for this study was the last visit in study A4091056, A4091057 or A4091058 or when the site notified of a planned TJR surgery.

Subject analysis set title	All Subjects
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received placebo matched to tanezumab in studies A4091056 and A4091057; received tanezumab SC injection of 2.5 mg or 2.5 mg/5 mg or 5 mg in studies A4091056, A4091057 or A4091058 and who received NSAID tablets (naproxen 500 mg, celecoxib 100 mg, or diclofenac extended release 75 mg) in study A4091058 and who had undergone a TJR surgery.

Primary: Number of Subjects With Surgeon's Assessment of Procedural Difficulty

End point title	Number of Subjects With Surgeon's Assessment of Procedural Difficulty[1]

End point description:

Following the TJR surgery on Day 1, the orthopedic surgeon was asked to answer the following question (Q): "taking into consideration the subject's medical history and physical condition prior to surgery would you classify the operative procedure as Uneventful, Minor complications or Major complications." Subjects were reported based on these categories for knee, hip and shoulder joint. Subjects may have been counted more than once if they had TJR surgery in more than one joint. Safety analysis set: all enrolled subjects of this study who had received at least one dose of SC study medication during studies A4091056, A4091057 or A4091058, and who had a qualifying i.e. total (not partial) joint replacement surgery. Here, 'number of subjects analysed (N)' = only those subjects who had data available for this endpoint. 'Number analysed (n)' = subjects evaluable for this endpoint at specified categories.

End point type	Primary

End point timeframe:

Day 1

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo	Tanezumab Combined	NSAID	All Subjects
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	17	92	13	122
Units: subjects				
Knee: Uneventful (n=9,51,8,68)	9	49	8	66
Knee: Minor Complications (n=9,51,8,68)	0	2	0	2
Knee: Major Complications (n=9,51,8,68)	0	0	0	0
Hip: Uneventful (n=8,41,4,53)	8	37	4	49
Hip: Minor Complications (n=8,41,4,53)	0	4	0	4
Hip: Major Complications (n=8,41,4,53)	0	0	0	0
Shoulder: Uneventful (n=0,0,1,1)	0	0	1	1
Shoulder: Minor Complications (n=0,0,1,1)	0	0	0	0
Shoulder: Major Complications (n=0,0,1,1)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Overall Satisfaction With Surgery as Assessed by the Self-Administered Patient Satisfaction (SAPS) Scale by Total Joint Replacement (TJR) at Week 24

End point title	Number of Subjects With Overall Satisfaction With Surgery as Assessed by the Self-Administered Patient Satisfaction (SAPS) Scale by Total Joint Replacement (TJR) at Week 24[2]

End point description:

SAPS has 4 questions; (Q1) How satisfied are you with the results of your surgery; results of surgery for improving (Q2) pain, (Q3) ability to do home/yard work, and (Q4) ability to do recreational activities. Items scored on a 4-point Likert scale with response of 'very satisfied' (100 points), 'somewhat satisfied' (75 points), 'somewhat dissatisfied' (50 points), and 'very dissatisfied' (25 points). Scale score=mean of scores of individual items, ranging from 25 to 100, higher scores= greater satisfaction. Here, number of subjects are summarized as, satisfied (very satisfied and somewhat satisfied categories combined) and dissatisfied (somewhat dissatisfied and very dissatisfied categories combined). Subjects may have been counted more than once if they had TJR surgery in more than one joint. Safety analysis set analyzed. 'N'=subjects who had data available for this endpoint. 'n'=subjects evaluable for this endpoint at specified categories.

End point type	Primary

End point timeframe:

Week 24

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo	Tanezumab Combined	NSAID	All Subjects
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	99	13	131
Units: subjects				
Knee: Q1: Satisfied (n=9,58,6,73)	9	53	5	67
Knee: Q1: Dissatisfied (n=9,58,6,73)	0	5	1	6

Knee: Q2: Satisfied (n=9,58,6,73)	9	52	5	66
Knee: Q2: Dissatisfied (n=9,58,6,73)	0	6	1	7
Knee: Q3: Satisfied (n=9,58,6,73)	9	48	5	62
Knee: Q3: Dissatisfied (n=9,58,6,73)	0	10	1	11
Knee: Q4: Satisfied (n=9,58,6,73)	9	50	5	64
Knee: Q4: Dissatisfied (n=9,58,6,73)	0	8	1	9
Hip: Q1: Satisfied (n=10,41,6,57)	9	40	6	55
Hip: Q1: Dissatisfied (n=10,41,6,57)	1	1	0	2
Hip: Q2: Satisfied (n=10,41,6,57)	9	41	6	56
Hip: Q2: Dissatisfied (n=10,41,6,57)	1	0	0	1
Hip: Q3: Satisfied (n=10,41,6,57)	9	41	6	56
Hip: Q3: Dissatisfied (n=10,41,6,57)	1	0	0	1
Hip: Q4: Satisfied (n=10,41,6,57)	9	40	6	55
Hip: Q4: Dissatisfied (n=10,41,6,57)	1	1	0	2
Shoulder: Q1: Satisfied (n=0,0,1,1)	0	0	1	1
Shoulder: Q1: Dissatisfied (n=0,0,1,1)	0	0	0	0
Shoulder: Q2: Satisfied (n=0,0,1,1)	0	0	1	1
Shoulder: Q2: Dissatisfied (n=0,0,1,1)	0	0	0	0
Shoulder: Q3: Satisfied (n=0,0,1,1)	0	0	1	1
Shoulder: Q3: Dissatisfied (n=0,0,1,1)	0	0	0	0
Shoulder:Q4: Satisfied (n=0,0,1,1)	0	0	1	1
Shoulder: Q4: Dissatisfied (n=0,0,1,1)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Post-Surgical Complications Upto Week 24

End point title	Number of Subjects with Post-Surgical Complications Upto Week 24[3]

End point description:

Post-surgical complications are adverse events occurring after TJR surgery that were considered clinically significant as assessed by investigator and attributable to the total joint replacement procedure. Subjects may have been counted more than once if they had TJR surgery in more than one joint. Safety analysis set: enrolled subjects who had received at least one dose of SC study medication during studies A4091056, A4091057 or A4091058, and who had a qualifying TJR surgery. 'n' = subjects evaluable for this endpoint at specified categories.

End point type	Primary

End point timeframe:

Baseline up to Week 24

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo	Tanezumab Combined	NSAID	All Subjects
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	20	113	17	150
Units: subjects				
Knee (n=10,66,9,85)	0	1	0	1
Hip (n=10,48,7,65)	0	5	0	5
Shoulder (n=0,0,1,1)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Additional or Corrective Procedures Related to Total Joint Replacement Upto Week 24

End point title	Number of Subjects With Additional or Corrective Procedures Related to Total Joint Replacement Upto Week 24[4]

End point description:

Subjects were asked whether they had been told by their orthopedic surgeon that additional or corrective procedures were necessary for their total joint replacement. Subjects, who responded as yes have been reported here. Subjects may have been counted more than once if they had TJR surgery in more than one joint. Safety analysis set: enrolled subjects who had received at least one dose of SC study medication during studies A4091056, A4091057 or A4091058, and who had a qualifying TJR surgery. 'n' = subjects evaluable for this endpoint at specified categories.

End point type	Primary

End point timeframe:

Baseline up to Week 24

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo	Tanezumab Combined	NSAID	All Subjects
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	20	113	17	150
Units: subjects				
Knee (n=10,66,9,85)	0	4	0	4
Hip (n=10,48,7,65)	0	5	1	6
Shoulder (n=0,0,1,1)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects who Participated in Physical Rehabilitation Activities Related to Total Joint Replacement Upto Week 24

End point title	Number of Subjects who Participated in Physical Rehabilitation Activities Related to Total Joint Replacement Upto Week 24[5]

End point description:

Subjects responded with a yes or no to the following question "are you participating in physical rehabilitation activities related to your replaced joint" Subjects responded with a yes, have been reported here. Subjects may have been counted more than once if they had TJR surgery in more than one joint. Safety analysis set: enrolled subjects who had received at least one dose of SC study medication during studies A4091056, A4091057 or A4091058, and who had a qualifying TJR surgery. 'n' = subjects evaluable for this endpoint at specified categories.

End point type	Primary

End point timeframe:

Baseline up to Week 24

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo	Tanezumab Combined	NSAID	All Subjects
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	20	113	17	150
Units: subjects				
Knee (n=10,66,9,85)	10	55	7	72
Hip (n=10,48,7,65)	9	33	3	45
Shoulder (n=0,0,1,1)	0	0	1	1

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Average Pain Score in to be Replaced or Replaced Joints at Week 24

End point title	Change From Baseline in Average Pain Score in to be Replaced or Replaced Joints at Week 24[6]

End point description:

Subjects assessed their average pain in to be replaced (pre-surgery) knee/ hip joint or in the replaced joint (post-surgery) in the past 24 hours using an 11-point numerical rating scale (NRS), ranging from 0 (no pain) to 10 (worst possible pain). Higher scores indicated higher pain. Change from baseline was calculated using the difference between post-baseline weekly mean and the baseline mean score. Subjects may have been counted more than once if they had TJR surgery in more than one joint. Safety analysis set: enrolled subjects who had received at least one dose of SC study medication during studies A4091056, A4091057 or A4091058, and who had a qualifying TJR surgery. 'n' = subjects evaluable for this endpoint at specified categories.

End point type	Primary

End point timeframe:

Baseline, Week 24

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo	Tanezumab Combined	NSAID	All Subjects
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	20	113	17	150
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline: Knee (n=10,71,10,91)	6.00 (± 2.31)	6.86 (± 2.14)	6.80 (± 2.20)	6.76 (± 2.16)
Baseline: Hip (n=10,48,7,65)	6.10 (± 2.13)	6.81 (± 2.27)	5.86 (± 3.44)	6.60 (± 2.38)
Change at Week 24: Knee (n=9,63,7,79)	-4.56 (± 1.24)	-5.32 (± 2.63)	-5.43 (± 2.51)	-5.24 (± 2.49)
Change at Week 24: Hip (n=10,42,6,58)	-5.20 (± 2.30)	-5.67 (± 2.37)	-5.00 (± 4.10)	-5.52 (± 2.53)

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain Subscale at Week 24

End point title	Change From Baseline in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain Subscale at Week 24[7]

End point description:

WOMAC: Self-administered, disease-specific questionnaire, which assesses clinically important, subject-relevant symptoms for pain, stiffness and physical function in subjects with osteoarthritis (OA). The WOMAC pain subscale is a 5-item questionnaire used to assess the amount of pain experienced due to OA of to be replaced/replaced index joint (knee or hip) during past 48 hours. It was calculated as the mean of scores from 5 individual questions. Scores for each question and WOMAC Pain subscale score on NRS ranged from 0 (no pain) to 10 (extreme pain), where higher scores indicated higher pain. Change from baseline was calculated using the difference between post-baseline weekly mean and the baseline mean score. Subjects may have been counted more than once if they had TJR surgery in more than one joint. Safety analysis set. Here, 'N' signifies only those subjects who had data available for this endpoint. 'n' = subjects evaluable for this endpoint at specified categories.

End point type	Primary

End point timeframe:

Baseline, Week 24

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo	Tanezumab Combined	NSAID	All Subjects
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	20	113	15	148
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline: Knee (n=10,68,9,87)	4.66 (± 3.05)	5.62 (± 2.33)	6.11 (± 2.31)	5.56 (± 2.41)
Baseline: Hip (n=10,46,6,62)	4.80 (± 2.61)	5.97 (± 2.46)	6.13 (± 1.98)	5.80 (± 2.45)
Change at Week 24: Knee (n=9,61,7,77)	-3.13 (± 1.74)	-4.50 (± 2.43)	-4.54 (± 3.15)	-4.34 (± 2.44)
Change at Week 24: Hip (n=10,40,5,55)	-4.34 (± 2.52)	-4.92 (± 2.62)	-5.92 (± 2.40)	-4.91 (± 2.57)

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Stiffness Subscale at Week 24

End point title	Change From Baseline in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Stiffness Subscale at Week 24[8]

End point description:

WOMAC: self-administered, disease-specific questionnaire, which assesses clinically important, subject-relevant symptoms for pain, stiffness and physical function in subjects with OA. Stiffness was defined as a sensation of decreased ease of movement in index joint (knee or hip). WOMAC stiffness subscale is a 2-item questionnaire used to assess amount of stiffness experienced due to OA in replaced/to be replaced index joint (knee or hip) during past 48 hours. It was calculated as mean of scores from 2 individual questions scored on NRS. Scores for each question and WOMAC stiffness subscale score on NRS ranged from 0 (no stiffness) to 10 (extreme stiffness), where higher scores indicated higher stiffness. Subjects may have been counted more than once if they had TJR surgery in more than one joint. Safety analysis set. Here, 'N' signifies only those subjects who had data available for this endpoint. 'n' = subjects evaluable for this endpoint at specified categories.

End point type	Primary

End point timeframe:

Baseline, Week 24

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo	Tanezumab Combined	NSAID	All Subjects
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	20	113	15	148
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline: Knee (n=10,68,9,87)	4.80 (± 2.78)	5.75 (± 2.52)	6.44 (± 2.58)	5.71 (± 2.55)
Baseline: Hip (10,46,6,62)	4.70 (± 2.75)	5.96 (± 2.69)	5.25 (± 3.50)	5.69 (± 2.77)
Change at Week 24: Knee (n=9,61,7,77)	-1.78 (± 1.52)	-4.13 (± 2.58)	-3.43 (± 3.13)	-3.79 (± 2.62)
Change at Week 24: Hip (n=10,40,5,55)	-4.00 (± 2.66)	-4.48 (± 2.87)	-3.80 (± 3.70)	-4.33 (± 2.86)

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Physical Function Subscale at Week 24

End point title	Change From Baseline in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Physical Function Subscale at Week 24[9]

End point description:

WOMAC: Self-administered, disease-specific questionnaire, which assesses clinically important, subject-relevant symptoms for pain, stiffness and physical function in subjects with OA. It refers to subject's ability to move around and perform usual activities of daily living. WOMAC physical function subscale=17-item questionnaire used to assess degree of difficulty experienced due to OA in replaced joint during past 48 hours. Calculated as mean of scores from 17 individual questions, which may not be a whole (integer) number, scored on an NRS. Scores for each question and WOMAC physical function subscale score ranged from 0 (no difficulty) to 10 (extreme difficulty), where higher scores=extreme difficulty/worse physical function. Subjects may have been counted more than once if they had TJR surgery in more than one joint. Safety analysis set. 'N'= only those subjects who had data available for this OM. 'n' = subjects evaluable for this OM at specified categories.

End point type	Primary

End point timeframe:

Baseline, Week 24

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo	Tanezumab Combined	NSAID	All Subjects
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	20	113	15	148
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline: Knee (n=10,68,9,87)	4.83 (± 2.99)	5.82 (± 2.11)	6.63 (± 1.98)	5.79 (± 2.23)
Baseline: Hip (n=10,46,6,62)	5.56 (± 2.21)	6.50 (± 2.22)	6.86 (± 1.48)	6.38 (± 2.17)
Change at Week 24: Knee (n=9,61,7,77)	-2.69 (± 1.51)	-4.42 (± 2.19)	-4.59 (± 2.90)	-4.24 (± 2.24)
Change at Week 24: Hip (n=10,40,5,55)	-4.64 (± 2.13)	-5.05 (± 2.44)	-5.95 (± 1.84)	-5.06 (± 2.33)

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Shoulder Pain and Disability Index (SPADI) Score at Week 24

End point title	Change From Baseline in Shoulder Pain and Disability Index (SPADI) Score at Week 24[10]

End point description:

SPADI:self-administered questionnaire to measure pain and disability associated with shoulder pathology.Pain dimension:5 questions,scores for each question ranged from 0=no pain to 10=worst pain imaginable,higher scores=extreme pain. Functional activities: 8 questions to measure degree of difficulty, scores for each question ranged from 0=no difficulty to 10=so difficult it requires help, higher scores=extreme difficulty. Pain and disability dimension score was calculated as sum of non-missing scores divided by the maximum possible score (50 [for pain] and 80 with no missing items [for disability]) multiplied by 100.Total score=mean of two dimensions, ranged from 0=best to 100=worst,higher scores indicated worsening of condition.Safety analysis set analysed who had qualifying shoulder replacement."N"=subjects who had data available for this endpoint. Data for arms placebo and tanezumab not reported as no subjects were evaluable. SD cannot be calculated and has been denoted as 99999.

End point type	Primary

End point timeframe:

Baseline, Week 24

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo	Tanezumab Combined	NSAID	All Subjects
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	0[11]	0[12]	1	1
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	()	()	89.88 (± 99999)	89.88 (± 99999)
Change at Week 24	()	()	-89.88 (± 99999)	-89.88 (± 99999)

Notes:

[11] - Data for arm placebo not reported as no subjects were evaluable for this endpoint.

[12] - Data for arm tanezumab not reported as no subjects were evaluable for this endpoint.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects who Used Concomitant Analgesic Medications

End point title	Number of Subjects who Used Concomitant Analgesic Medications[13]

End point description:

End point type	Primary

End point timeframe:

Baseline up to Week 24

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint

End point values	Placebo	Tanezumab Combined	NSAID	All Subjects
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	20	113	17	150
Units: subjects	18	100	15	133

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 24

Adverse event reporting additional description:

Same event may appear as both an adverse event (AE) and serious AE. What is presented are distinct events. An event may be categorized as serious in one and as non-serious in another or one subject may have experienced both serious and non-serious event. Safety set analyzed. AEs for tanezumab were collected and reported dose wise and combined.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects who received placebo matched to tanezumab in studies A4091056 (NCT02697773) and A4091057 (NCT02709486) and who had undergone a TJR surgery, were followed up for a maximum duration of 24 weeks in this study. Baseline for this study was the last visit in study A4091056, A4091057 or A4091058 (NCT02528188) or when the site notified of a planned TJR surgery.

Reporting group title	Tanezumab Combined

Reporting group description:

Subjects who received tanezumab SC injection of 2.5 mg or 2.5 mg/5 mg or 5 mg in studies A4091056, A4091057 or A4091058 and who had undergone a TJR surgery, were followed up for a maximum duration of 24 weeks in this study. Baseline for this study was the last visit in study A4091056, A4091057 or A4091058 or when the site notified of a planned TJR surgery.

Reporting group title	NSAID

Reporting group description:

Subjects who received NSAID tablets (naproxen 500 mg, celecoxib 100 mg, or diclofenac extended release 75 mg) in study A4091058 and who had undergone a TJR surgery, were followed up for a maximum duration of 24 weeks in this study. Baseline for this study was the last visit in study A4091056, A4091057 or A4091058 or when the site notified of a planned TJR surgery.

Reporting group title	All Subjects

Reporting group description:

All subjects who received placebo matched to tanezumab in studies A4091056 and A4091057; received tanezumab SC injection of 2.5 mg or 2.5 mg/5 mg or 5 mg in studies A4091056, A4091057 or A4091058 and who received NSAID tablets (naproxen 500 mg, celecoxib 100 mg, or diclofenac extended release 75 mg) in study A4091058 and who had undergone a TJR surgery.

Reporting group title	Tanezumab 2.5 mg

Reporting group description:

Subjects who received tanezumab 2.5 mg SC injection in studies A4091056, A4091057 or A4091058 and who had undergone a TJR surgery, were followed up for a maximum duration of 24 weeks in this study. Baseline for this study was the last visit in study A4091056, A4091057 or A4091058 or when the site notified of a planned TJR surgery.

Reporting group title	Tanezumab 2.5/5 mg

Reporting group description:

Subjects who received tanezumab 2.5/5 mg SC injection in study A4091056 and who had undergone a TJR surgery, were followed up for a maximum duration of 24 weeks in this study. Baseline for this study was the last visit in study A4091056, A4091057 or A4091058 or when the site notified of a planned TJR surgery.

Reporting group title	Tanezumab 5 mg

Reporting group description:

Subjects who received tanezumab 5 mg SC injection in studies A4091057 or A4091058 and who had undergone a TJR surgery, were followed up for a maximum duration of 24 weeks in this study. Baseline for this study was the last visit in study A4091056, A4091057 or A4091058 or when the site notified of a planned TJR surgery.

Serious adverse events	Placebo	Tanezumab Combined	NSAID
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	15 / 113 (13.27%)	2 / 17 (11.76%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Transitional cell carcinoma			
subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	0 / 17 (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
Injury, poisoning and procedural complications			
Periprosthetic fracture			
subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	0 / 17 (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
Tendon rupture			
subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	0 / 17 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	0 / 17 (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
Haematoma			
subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	0 / 17 (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
Cardiac disorders			
Coronary artery occlusion			

subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	0 / 17 (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
Nervous system disorders			
Parkinson's disease			
subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	0 / 17 (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
Gastrointestinal disorders			
Colitis ischaemic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	0 / 17 (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
Diarrhoea			
subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	0 / 17 (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
Enteritis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	0 / 17 (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
Hiatus hernia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	0 / 17 (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			
Cholecystitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	0 / 17 (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
Psychiatric disorders			
Hallucination			

subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	0 / 17 (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			
Osteoarthritis			
subjects affected / exposed	0 / 20 (0.00%)	3 / 113 (2.65%)	2 / 17 (11.76%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	0 / 17 (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
Gastroenteritis viral			
subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	0 / 17 (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
Pneumonia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	0 / 17 (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
Post procedural infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	0 / 17 (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
Product issues			
Device dislocation			
subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	0 / 17 (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

Serious adverse events	All Subjects	Tanezumab 2.5 mg	Tanezumab 2.5/5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 150 (11.33%)	5 / 52 (9.62%)	3 / 8 (37.50%)

number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Transitional cell carcinoma			
subjects affected / exposed	1 / 150 (0.67%)	0 / 52 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Periprosthetic fracture			
subjects affected / exposed	1 / 150 (0.67%)	1 / 52 (1.92%)	0 / 8 (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
Tendon rupture			
subjects affected / exposed	1 / 150 (0.67%)	0 / 52 (0.00%)	0 / 8 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 150 (0.67%)	1 / 52 (1.92%)	0 / 8 (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
Haematoma			
subjects affected / exposed	1 / 150 (0.67%)	1 / 52 (1.92%)	0 / 8 (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
Cardiac disorders			
Coronary artery occlusion			
subjects affected / exposed	1 / 150 (0.67%)	1 / 52 (1.92%)	0 / 8 (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
Nervous system disorders			
Parkinson's disease			
subjects affected / exposed	1 / 150 (0.67%)	0 / 52 (0.00%)	0 / 8 (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

Gastrointestinal disorders			
Colitis ischaemic			
subjects affected / exposed	1 / 150 (0.67%)	0 / 52 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 150 (0.67%)	1 / 52 (1.92%)	0 / 8 (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
Enteritis			
subjects affected / exposed	1 / 150 (0.67%)	1 / 52 (1.92%)	0 / 8 (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
Hiatus hernia			
subjects affected / exposed	1 / 150 (0.67%)	0 / 52 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 150 (0.67%)	0 / 52 (0.00%)	0 / 8 (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
Psychiatric disorders			
Hallucination			
subjects affected / exposed	1 / 150 (0.67%)	0 / 52 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	5 / 150 (3.33%)	1 / 52 (1.92%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Device related infection			

subjects affected / exposed	1 / 150 (0.67%)	0 / 52 (0.00%)	0 / 8 (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
Gastroenteritis viral			
subjects affected / exposed	1 / 150 (0.67%)	0 / 52 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 150 (0.67%)	0 / 52 (0.00%)	0 / 8 (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
Post procedural infection			
subjects affected / exposed	1 / 150 (0.67%)	1 / 52 (1.92%)	0 / 8 (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
Product issues			
Device dislocation			
subjects affected / exposed	1 / 150 (0.67%)	0 / 52 (0.00%)	0 / 8 (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

Serious adverse events	Tanezumab 5 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 53 (13.21%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Transitional cell carcinoma			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Periprosthetic fracture			

subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tendon rupture				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Deep vein thrombosis				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematoma				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Coronary artery occlusion				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Parkinson's disease				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Colitis ischaemic				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				

subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enteritis				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hiatus hernia				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Hallucination				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Osteoarthritis				
subjects affected / exposed	2 / 53 (3.77%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Device related infection				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				

subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural infection			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device dislocation			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	Tanezumab Combined	NSAID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	21 / 113 (18.58%)	4 / 17 (23.53%)
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	0 / 20 (0.00%)	9 / 113 (7.96%)	0 / 17 (0.00%)
occurrences (all)	0	10	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 113 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Cardiac disorders			
Atrioventricular block second degree			
subjects affected / exposed	0 / 20 (0.00%)	0 / 113 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Coronary artery stenosis			

subjects affected / exposed	0 / 20 (0.00%)	0 / 113 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 113 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Peripheral swelling			
subjects affected / exposed	0 / 20 (0.00%)	0 / 113 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 20 (0.00%)	0 / 113 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 20 (0.00%)	2 / 113 (1.77%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 20 (0.00%)	3 / 113 (2.65%)	0 / 17 (0.00%)
occurrences (all)	0	3	0
Joint swelling			
subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Osteoarthritis			
subjects affected / exposed	0 / 20 (0.00%)	3 / 113 (2.65%)	0 / 17 (0.00%)
occurrences (all)	0	3	0
Spinal osteoarthritis			
subjects affected / exposed	0 / 20 (0.00%)	2 / 113 (1.77%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Tendonitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 113 (0.88%)	1 / 17 (5.88%)
occurrences (all)	0	1	1

Non-serious adverse events	All Subjects	Tanezumab 2.5 mg	Tanezumab 2.5/5 mg
Total subjects affected by non-serious adverse events			

subjects affected / exposed	25 / 150 (16.67%)	9 / 52 (17.31%)	3 / 8 (37.50%)
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	9 / 150 (6.00%)	3 / 52 (5.77%)	0 / 8 (0.00%)
occurrences (all)	10	3	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 150 (0.67%)	0 / 52 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrioventricular block second degree			
subjects affected / exposed	1 / 150 (0.67%)	0 / 52 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Coronary artery stenosis			
subjects affected / exposed	1 / 150 (0.67%)	0 / 52 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 150 (0.67%)	0 / 52 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	1 / 150 (0.67%)	0 / 52 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 150 (0.67%)	0 / 52 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	2 / 150 (1.33%)	0 / 52 (0.00%)	1 / 8 (12.50%)
occurrences (all)	2	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 150 (2.00%)	0 / 52 (0.00%)	1 / 8 (12.50%)
occurrences (all)	3	0	1
Joint swelling			

subjects affected / exposed	2 / 150 (1.33%)	1 / 52 (1.92%)	0 / 8 (0.00%)
occurrences (all)	2	1	0
Osteoarthritis			
subjects affected / exposed	3 / 150 (2.00%)	3 / 52 (5.77%)	0 / 8 (0.00%)
occurrences (all)	3	3	0
Spinal osteoarthritis			
subjects affected / exposed	2 / 150 (1.33%)	1 / 52 (1.92%)	1 / 8 (12.50%)
occurrences (all)	2	1	1
Tendonitis			
subjects affected / exposed	2 / 150 (1.33%)	1 / 52 (1.92%)	0 / 8 (0.00%)
occurrences (all)	2	1	0

Non-serious adverse events	Tanezumab 5 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 53 (16.98%)		
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	6 / 53 (11.32%)		
occurrences (all)	7		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Atrioventricular block second degree			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences (all)	0		
Coronary artery stenosis			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences (all)	0		
Peripheral swelling			

subjects affected / exposed occurrences (all)	0 / 53 (0.00%) 0		
Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all)	 0 / 53 (0.00%) 0		
Renal and urinary disorders Urinary retention subjects affected / exposed occurrences (all)	 1 / 53 (1.89%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Joint swelling subjects affected / exposed occurrences (all) Osteoarthritis subjects affected / exposed occurrences (all) Spinal osteoarthritis subjects affected / exposed occurrences (all) Tendonitis subjects affected / exposed occurrences (all)	 2 / 53 (3.77%) 2 0 / 53 (0.00%) 0 0 / 53 (0.00%) 0 0 / 53 (0.00%) 0 0 / 53 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

For ‘age group breakdown of trial’ 2 subjects have incorrectly been placed under ‘elderly 85 years and over’, due to database limitation. The age for these 2 subjects are ‘unspecified’ as correctly captured under ‘age characteristics’

Notes: