



Clinical trial results:

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

Summary

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

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 |
| This version publication date | 09 July 2022 |
| First version publication date | 09 July 2022 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | A4091061 |
|-----------------------|----------|

Additional study identifiers

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

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 21 October 2021 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 25 June 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

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

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Argentina: 1 |
| Country: Number of subjects enrolled | Australia: 1 |
| Country: Number of subjects enrolled | Austria: 1 |
| Country: Number of subjects enrolled | Brazil: 7 |
| Country: Number of subjects enrolled | Chile: 6 |
| Country: Number of subjects enrolled | China: 17 |
| Country: Number of subjects enrolled | Czechia: 1 |
| Country: Number of subjects enrolled | Hungary: 4 |
| Country: Number of subjects enrolled | Japan: 11 |
| Country: Number of subjects enrolled | Korea, Republic of: 7 |
| Country: Number of subjects enrolled | Poland: 50 |
| Country: Number of subjects enrolled | Romania: 22 |
| Country: Number of subjects enrolled | Slovakia: 17 |
| Country: Number of subjects enrolled | Spain: 5 |
| Country: Number of subjects enrolled | United Kingdom: 5 |
| Worldwide total number of subjects | 155 |
| EEA total number of subjects | 100 |

Notes:

| Subjects enrolled per age group | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 96 |
| From 65 to 84 years | 59 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

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

Pre-assignment

Screening details:

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

Period 1

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

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

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

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

Dosage and administration details:

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

| | |
|------------------|-----------------|
| Arm title | Tanezumab 10 mg |
|------------------|-----------------|

Arm description:

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

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

Dosage and administration details:

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

| | |
|------------------|--------------------|
| Arm title | Tanezumab 10/20 mg |
|------------------|--------------------|

Arm description:

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

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

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

Dosage and administration details:

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

| | |
|------------------|-----------------|
| Arm title | Tanezumab 20 mg |
|------------------|-----------------|

Arm description:

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

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

Dosage and administration details:

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

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

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

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

Baseline characteristics

Reporting groups

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

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

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

| | | | |
|---------------------------|--------|-----|--|
| >=45 to <65 years | 33 | 82 | |
| >=65 years | 36 | 59 | |
| | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 63.5 | | |
| standard deviation | ± 10.1 | - | |
| Sex: Female, Male | | | |
| Units: Subjects | | | |
| Female | 26 | 69 | |
| Male | 46 | 86 | |
| Race | | | |
| Units: Subjects | | | |
| Asian | 16 | 35 | |
| Black or African American | 1 | 2 | |
| White | 55 | 118 | |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 5 | 15 | |
| Not Hispanic or Latino | 67 | 140 | |

End points

End points reporting groups

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

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

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

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

Statistical analyses

| Statistical analysis title | Placebo vs Tanezumab 20mg |
|---|---------------------------------------|
| Statistical analysis description: | |
| Change at Week 8: Analysis of covariance (ANCOVA) model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 145 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0381 |
| Method | ANCOVA |
| Parameter estimate | Differences in least square (LS) mean |
| Point estimate | -0.78 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.52 |
| upper limit | -0.04 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.37 |

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

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

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

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

Statistical analyses

| Statistical analysis title | Placebo vs Tanezumab 20mg |
|--|----------------------------|
| Statistical analysis description: | |
| Change at Week 1: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 145 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0497 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.36 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.72 |
| upper limit | 0 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.18 |

| Statistical analysis title | Placebo vs Tanezumab 20mg |
|--|---------------------------|
| Statistical analysis description: | |
| Change at Week 2: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

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

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

End point description:

Daily worst pain intensity assessed by subjects: 11 point pain intensity NRS. Range: 0 (no pain) to 10 (worst possible pain). Higher scores: more severe pain. Subjects noted pain: past 24 hours (0 to 10) on IRT diaries. Baseline daily worst pain intensity: mean of daily worst pain intensity NRS score during baseline assessment period (up to 5 days prior to dosing) before randomisation. Wk 1, 2, 4, 6, 8, 12, 16, 24 daily worst pain intensity value: mean of daily worst pain intensity NRS scores noted for 7 days prior to each wk. 99999 = summarised data not available. Individual values: each wk: 10mg: 0.4, 0.2, -2.85, -0.4, -1.8, -0.4, 0, 0.45, 0, 0.4, -0.08, -4, -0.25, -2.37, -0.4, 0, 0.6, 0, -0.02, -0.51, -1.85, -0.4, -4.08, -1.4, 0, 0.02, -1.14,

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

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 1, 2, 4, 6, 8, 12, 16 and 24 | |

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

Statistical analyses

| | |
|---|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 1: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 145 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.1103 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.33 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.73 |
| upper limit | 0.07 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.2 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|---|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 6: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 145 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0155 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.88 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.59 |
| upper limit | -0.17 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.36 |

| | |
|---|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 8: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 145 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0505 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.52 |
| upper limit | 0 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.38 |

| | |
|--|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 12: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 145 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0761 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.52 |
| upper limit | 0.08 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.4 |

| | |
|--|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 16: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 145 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.1263 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.74 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.7 |
| upper limit | 0.21 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.48 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

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

Statistical analyses

| Statistical analysis title | Placebo vs Tanezumab 20mg |
|--|----------------------------|
| Statistical analysis description: | |
| Change at Week 1: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 55 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.3003 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.47 |
| upper limit | 0.47 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.48 |

| Statistical analysis title | Placebo vs Tanezumab 20mg |
|--|---------------------------|
| Statistical analysis description: | |
| Change at Week 2: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

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

Statistical analyses

| Statistical analysis title | Placebo vs Tanezumab 20mg |
|--|----------------------------|
| Statistical analysis description: | |
| Change at Week 1: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the non-index cancer pain sites and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 55 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0575 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -1.07 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.17 |
| upper limit | 0.04 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.54 |

| Statistical analysis title | Placebo vs Tanezumab 20mg |
|--|---------------------------|
| Statistical analysis description: | |
| Change at Week 2: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the non-index cancer pain sites and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 55 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0031 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -1.96 |

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

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

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Notes:

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

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 1, 2, 4, 6, 8, 12, 16 and 24 | |

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

Notes:

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

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

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

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

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Brief Pain Inventory Short Form (BPI-sf) Average Pain Scores at Weeks 2, 4, 8, 16 and 24

| | |
|-----------------|--|
| End point title | Change From Baseline in the Brief Pain Inventory Short Form (BPI-sf) Average Pain Scores at Weeks 2, 4, 8, 16 and 24 |
|-----------------|--|

End point description:

BPI-sf was a self-administered questionnaire used to assess the severity of pain and the impact of pain on daily functions during a 24 hour period prior to evaluation at specified/scheduled time points. Subjects recorded a score from range 0 (no pain) to 10 (pain as bad as you can imagine) on IRT diaries, which best described their average pain in the last 24 hours at specified time points. Higher scores signified worse pain. 99999=summarised data not available. Individual values at wk2,4,8,16,24 for 10mg:-2,0,-5,0,-3,-1,0,-1,0,-1,-1,-3,-2,-4,-1,-1,-1,-2,-4,-2,-3,-4,-5,-2,-3,-1,-2,-6,-3,-4,0,-3,-3,-6,-2,-6,0,2,-3, for10/20mg: 0,-2,-2. 99999=no subjects. Here, 'N': subjects evaluable for this end point, 'n': subjects evaluable at specified time points.

| | |
|------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 2, 4, 8, 16 and 24 | |

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|-------------------------------------|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 1 | 71 |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Week 2 (n=73,9,1,71) | -0.70 (± 0.30) | 99999 (± 99999) | 99999 (± 99999) | -1.10 (± 0.31) |

| | | | | |
|---------------------------------|----------------|-----------------|-----------------|----------------|
| Change at Week 4 (n=73,9,1,71) | -1.04 (± 0.32) | 99999 (± 99999) | 99999 (± 99999) | -1.81 (± 0.33) |
| Change at Week 8 (n=73,9,1,71) | -1.05 (± 0.35) | 99999 (± 99999) | 99999 (± 99999) | -1.82 (± 0.35) |
| Change at Week 16 (n=73,6,1,71) | -0.86 (± 0.39) | 99999 (± 99999) | 99999 (± 99999) | -1.63 (± 0.42) |
| Change at Week 24 (n=73,9,1,71) | -0.62 (± 0.44) | 99999 (± 99999) | 99999 (± 99999) | -1.31 (± 0.43) |

Statistical analyses

| Statistical analysis title | Placebo vs Tanezumab 20mg |
|---|----------------------------|
| Statistical analysis description: | |
| Change at Week 2: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline BPI-sf, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.2091 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.03 |
| upper limit | 0.23 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.32 |

| Statistical analysis title | Placebo vs Tanezumab 20mg |
|---|---------------------------|
| Statistical analysis description: | |
| Change at Week 4: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline BPI-sf, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0244 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.77 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.44 |
| upper limit | -0.1 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.34 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0401 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.78 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.52 |
| upper limit | -0.04 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.37 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0716 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.77 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.61 |
| upper limit | 0.07 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.42 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.1133 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.69 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.55 |
| upper limit | 0.17 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.43 |

Secondary: Change From Baseline in the BPI-sf Worst Pain Scores at Weeks 2, 4, 8, 16 and 24

| | |
|-----------------|--|
| End point title | Change From Baseline in the BPI-sf Worst Pain Scores at Weeks 2, 4, 8, 16 and 24 |
|-----------------|--|

End point description:

BPI-sf was a self-administered questionnaire used to assess the severity of pain and the impact of pain on daily functions during a 24 hour period prior to evaluation. Subjects recorded a score from range 0 (no pain) to 10 (pain as bad as you can imagine) on IRT diaries, which best described their worst pain in the last 24 hours at specified time points. Higher scores signified worse pain. 99999=summarised data not available. Individual values at wk2,4,8,16,24 for 10mg:--1,0,-5,0,-1,-2,0,-1,0, 0,-1,-2,-1,-5,-2,-1,0,-2, -3,-1,-2,-4,-5,-3,-3,-1,-2,-6,-3,-4,-1,-6,-3, -6,-2,-7,-1,1,-3 for10/20mg: -1,-2,-2. 99999=no subjects. Here, 'N': subjects evaluable for this end point, 'n': subjects evaluable at specified time points.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|-------------------------------------|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 1 | 71 |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Week 2 (n=73, 9,1,71) | -0.69 (± 0.30) | 99999 (± 99999) | 99999 (± 99999) | -1.11 (± 0.33) |
| Change at Week 4 (n=73, 9,1,71) | -0.97 (± 0.32) | 99999 (± 99999) | 99999 (± 99999) | -1.72 (± 0.34) |
| Change at Week 8 (n=73, 9,1,71) | -1.07 (± 0.37) | 99999 (± 99999) | 99999 (± 99999) | -1.87 (± 0.39) |
| Change at Week 16 (n=73, 6,1,71) | -0.92 (± 0.41) | 99999 (± 99999) | 99999 (± 99999) | -1.79 (± 0.43) |
| Change at Week 24 (n=73, 6,1,71) | -0.56 (± 0.41) | 99999 (± 99999) | 99999 (± 99999) | -1.45 (± 0.42) |

Statistical analyses

| Statistical analysis title | Placebo vs Tanezumab 20mg |
|---|----------------------------|
| Statistical analysis description: | |
| Change at Week 2: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline BPI-sf, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.2037 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.09 |
| upper limit | 0.23 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.33 |

| Statistical analysis title | Placebo vs Tanezumab 20mg |
|---|---------------------------|
| Statistical analysis description: | |
| Change at Week 4: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline BPI-sf, and baseline average pain intensity at the index bone metastasis cancer pain site and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0355 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.45 |
| upper limit | -0.05 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.35 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0524 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.6 |
| upper limit | 0.01 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.41 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

| | |
|---|----------------------------|
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0607 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.87 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.77 |
| upper limit | 0.04 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.46 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0438 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.89 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.75 |
| upper limit | -0.03 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.43 |

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

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

End point description:

Daily avg pain intensity in index bone metastasis cancer pain site assessed by subjects: 11 point pain intensity NRS. Range: 0 (no pain) to 10 (worst possible pain), higher scores = more severe pain. Subjects recorded daily average pain at painful site during the past 24 hours by choosing the appropriate number from 0 to 10 on IRT diaries. Wk 1, 2, 4, 6, 8, 12, 16 and 24 pain intensity value = mean of the daily avg pain intensity NRS scores for the 7 days prior to each week. Number of subjects with cumulative

reduction of $\geq 30, 50, 70, 90$ % in daily avg pain intensity NRS score in the index bone metastasis cancer pain site from Baseline to Wk 1, 2, 4, 6, 8, 12, 16 and 24 were reported. Subjects might be reported more than once in the specified rows for a time point. Rows with only non-zero data for cumulative reduction at specified time points, for at least 1 reporting arm, are reported below. Here, 'N': subjects evaluable for this end point and 'n': subjects evaluable at specific time points.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 1, 2, 4, 6, 8, 12, 16 and 24 | |

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

| | | | | |
|--|----|---|---|----|
| Week 12: Reduction of $\geq 90\%$ (n=73,9,1,71) | 2 | 0 | 0 | 5 |
| Week 16: Reduction of $\geq 30\%$ (n=73,7,1,71) | 17 | 2 | 0 | 27 |
| Week 16: Reduction of $\geq 50\%$ (n=73,9,1,71) | 12 | 2 | 0 | 19 |
| Week 16: Reduction of $\geq 70\%$ (n=73,9,1,71) | 7 | 1 | 0 | 12 |
| Week 16: Reduction of $\geq 90\%$ (n=73,9,1,71) | 5 | 0 | 0 | 5 |
| Week 24: Reduction of $\geq 30\%$ (n=73,6,1,71) | 16 | 4 | 0 | 27 |
| Week 24: Reduction of $\geq 50\%$ (n=73,9,1,71) | 10 | 3 | 0 | 19 |
| Week 24: Reduction of $\geq 70\%$ (n=73,9,1,71) | 5 | 2 | 0 | 11 |
| Week 24: Reduction of $\geq 90\%$ (n=73,9,1,71) | 3 | 1 | 0 | 4 |

Statistical analyses

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

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.9565 |
| Method | Regression, Logistic |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

Statistical analysis title

Placebo vs Tanezumab 20mg

Statistical analysis description:

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

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

Statistical analysis title

Placebo vs Tanezumab 20mg

Statistical analysis description:

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

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

Statistical analysis title

Placebo vs Tanezumab 20mg

Statistical analysis description:

Week 4 Reduction $\geq 30\%$: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables

(concomitant anticancer treatment and tumor aggressiveness).

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

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

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

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.03 |
| upper limit | 24.16 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

Statistical analysis title

Placebo vs Tanezumab 20mg

Statistical analysis description:

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

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0405 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.55 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.04 |
| upper limit | 6.22 |

Statistical analysis title

Placebo vs Tanezumab 20mg

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

| | |
|---|----------------------|
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0993 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.21 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.8 |
| upper limit | 12.83 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.1726 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 4.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.51 |
| upper limit | 43.64 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0918 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.84 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.91 |
| upper limit | 3.74 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0704 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.13 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.94 |
| upper limit | 4.82 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

Statistical analysis title

Placebo vs Tanezumab 20mg

Statistical analysis description:

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

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

Statistical analysis title

Placebo vs Tanezumab 20mg

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.8867 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.91 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.24 |
| upper limit | 3.46 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0689 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.95 |
| upper limit | 4.21 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

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

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

End point description:

Daily worst pain intensity in index bone metastasis cancer pain site assessed by subjects: 11 point pain intensity NRS. Range: 0 (no pain) to 10 (worst possible pain), higher scores = more severe pain. Subjects recorded daily worst pain at painful site during past 24 hours by choosing appropriate number from 0 to 10 on IRT diaries. Wk 1, 2, 4, 6, 8, 12, 16 and 24 pain intensity value = mean of the daily worst pain intensity NRS scores for the 7 days prior to each wk. Number of subjects with cumulative reduction of

>= 30,50,70,90 % in daily worst pain intensity NRS score in the index bone metastasis cancer pain site from Baseline to Wk 1, 2, 4, 6, 8, 12, 16 and 24 were reported. Subjects might be reported more than once in the specified rows for a time point. Rows with only non-zero data for cumulative reduction at specified time points, for at least 1 reporting arm, are reported below. Here, 'N': subjects evaluable for this end point and 'n': subjects evaluable at specific time points.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 1, 2, 4, 6, 8, 12, 16 and 24 | |

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|-----------------------------|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 0 ^[9] | 71 |
| Units: Subjects | | | | |
| Week 1: Reduction of >=30% | 7 | 2 | | 9 |
| Week 1: Reduction of >=50% | 1 | 0 | | 3 |
| Week 1: Reduction of >=70% | 0 | 0 | | 2 |
| Week 1: Reduction of >=90% | 0 | 0 | | 0 |
| Week 2: Reduction of >=30% | 9 | 2 | | 17 |
| Week 2: Reduction of >=50% | 2 | 1 | | 8 |
| Week 2: Reduction of >=70% | 0 | 0 | | 5 |
| Week 2: Reduction of >=90% | 0 | 0 | | 2 |
| Week 4: Reduction of >=30% | 12 | 1 | | 21 |
| Week 4: Reduction of >=50% | 5 | 1 | | 14 |
| Week 4: Reduction of >=70% | 0 | 1 | | 6 |
| Week 4: Reduction of >=90% | 0 | 0 | | 2 |
| Week 6: Reduction of >=30% | 13 | 4 | | 26 |
| Week 6: Reduction of >=50% | 4 | 1 | | 14 |
| Week 6: Reduction of >=70% | 2 | 0 | | 7 |
| Week 6: Reduction of >=90% | 0 | 0 | | 2 |
| Week 8: Reduction of >=30% | 14 | 5 | | 24 |
| Week 8: Reduction of >=50% | 7 | 2 | | 16 |
| Week 8: Reduction of >=70% | 2 | 0 | | 8 |
| Week 8: Reduction of >=90% | 2 | 0 | | 2 |
| Week 12: Reduction of >=30% | 16 | 5 | | 24 |
| Week 12: Reduction of >=50% | 8 | 2 | | 16 |
| Week 12: Reduction of >=70% | 5 | 1 | | 7 |
| Week 12: Reduction of >=90% | 2 | 0 | | 4 |
| Week 16: Reduction of >=30% | 11 | 2 | | 24 |
| Week 16: Reduction of >=50% | 9 | 2 | | 18 |
| Week 16: Reduction of >=70% | 7 | 0 | | 11 |
| Week 16: Reduction of >=90% | 3 | 0 | | 3 |
| Week 24: Reduction of >=30% | 11 | 4 | | 25 |
| Week 24: Reduction of >=50% | 9 | 3 | | 18 |
| Week 24: Reduction of >=70% | 4 | 2 | | 9 |
| Week 24: Reduction of >=90% | 2 | 0 | | 3 |

Notes:

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

Statistical analyses

| | |
|--|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 1 Reduction $\geq 30\%$: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness). | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.6658 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.27 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.43 |
| upper limit | 3.7 |

| | |
|--|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 1 Reduction $\geq 50\%$: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness). | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.3443 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.07 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.3 |
| upper limit | 31.35 |

| | |
|--|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 1 Reduction $\geq 70\%$: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness). | |
| Comparison groups | Placebo v Tanezumab 20 mg |

| | |
|---|----------------------|
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.9527 |
| Method | Regression, Logistic |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0757 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.25 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.92 |
| upper limit | 5.5 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|--|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 4 Reduction $\geq 90\%$: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness). | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.9493 |
| Method | Regression, Logistic |

| | |
|--|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 4 Reduction $\geq 70\%$: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness). | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.9538 |
| Method | Regression, Logistic |

| | |
|--|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 4 Reduction $\geq 50\%$: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness). | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0359 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.22 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.08 |
| upper limit | 9.61 |

| | |
|--|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 6 Reduction $\geq 30\%$: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness). | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0143 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.66 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.22 |
| upper limit | 5.8 |

| | |
|--|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 6 Reduction $\geq 50\%$: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness). | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0176 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 4.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.28 |
| upper limit | 13.74 |

| | |
|--|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 6 Reduction $\geq 90\%$: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness). | |
| Comparison groups | Placebo v Tanezumab 20 mg |

| | |
|---|----------------------|
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.9493 |
| Method | Regression, Logistic |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|--|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 8 Reduction $\geq 30\%$: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness). | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0527 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.99 |
| upper limit | 4.67 |

| | |
|--|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 8 Reduction $\geq 70\%$: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness). | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0994 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.91 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.77 |
| upper limit | 19.76 |

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0742 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.35 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.92 |
| upper limit | 6.01 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.146 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.76 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.82 |
| upper limit | 3.75 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.5565 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.44 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.42 |
| upper limit | 4.91 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|---|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 16 Reduction $\geq 30\%$: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness). | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0116 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.27 |
| upper limit | 6.47 |

| | |
|---|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 16 Reduction $\geq 50\%$: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness). | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0615 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.34 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.96 |
| upper limit | 5.7 |

| | |
|---|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 16 Reduction $\geq 70\%$: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness). | |
| Comparison groups | Placebo v Tanezumab 20 mg |

| | |
|---|----------------------|
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.3316 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.68 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.59 |
| upper limit | 4.8 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0513 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.42 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1 |
| upper limit | 5.88 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0083 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.33 |
| upper limit | 6.76 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|---|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 24 Reduction $\geq 90\%$: Logistic regression model included baseline average pain intensity at the index bone metastasis cancer pain site, baseline worst pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness). | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.7251 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.41 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.21 |
| upper limit | 9.65 |

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

| | | | | |
|--------------------------------|---------------------|----------------------|----------------------|---------------------|
| Change at Week 16 (n=73,071,6) | -0.16 (\pm 0.16) | 99999 (\pm 99999) | 99999 (\pm 99999) | -0.32 (\pm 0.17) |
| Change at Week 24 (n=73,071,6) | -0.19 (\pm 0.18) | 99999 (\pm 99999) | 99999 (\pm 99999) | -0.29 (\pm 0.17) |

Statistical analyses

| Statistical analysis title | Placebo vs Tanezumab 20mg |
|---|----------------------------|
| Statistical analysis description: | |
| Change at Week 2: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline global assessment score, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.7045 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.28 |
| upper limit | 0.19 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.12 |

| Statistical analysis title | Placebo vs Tanezumab 20mg |
|---|---------------------------|
| Statistical analysis description: | |
| Change at Week 4: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline global assessment score, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0402 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.59 |
| upper limit | -0.01 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.14 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0637 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.33 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.67 |
| upper limit | 0.02 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.17 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|--|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 24: ANCOVA model for imputed datasets included treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline global assessment score, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.5894 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.47 |
| upper limit | 0.27 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.18 |

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

| | |
|---|---|
| End point title | Number of Subjects With Reduction of ≥ 2 Points From Baseline in PGA-CP Scores at Weeks 2, 4, 8, 16 and 24 |
| End point description: | |
| Subjects at specified time points, answered to the following question, "Considering all the way your cancer pain affects you, how are you doing today?" on a Likert scale ranging from 1 to 5, on IRT diaries. Scores: 1= very good (asymptomatic and no limitation of normal activities); 2= good(mild symptoms and no limitation of normal activities); 3= fair(moderate symptoms and limitation of some normal activities); 4= poor (severe symptoms and inability to carry out most normal activities); and 5= very poor (very severe symptoms which are intolerable and inability to carry out all normal activities). Higher scores: worsening of condition. Efficacy data from subjects who were originally randomised to tanezumab 10 mg arm were not included in analyses of efficacy as pre-specified in protocol. So, summarised data is not reported for tanezumab 10 mg and 10/20 mg arms. Reported individual values. Here, 'n': subjects evaluable at specified time points. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 2, 4, 8, 16 and 24 | |

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

Statistical analyses

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

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

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.41 |
| upper limit | 3.41 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

Week 8: Logistic regression model included baseline PGA-CP, baseline average pain intensity at the index bone metastasis cancer pain site, treatment, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness).

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 145 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.6894 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.23 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.44 |
| upper limit | 3.43 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 145 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.8354 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.38 |
| upper limit | 3.35 |

Secondary: Change From Baseline in BPI-sf Pain Interference With Enjoyment of Life at Weeks 2, 4, 8, 16 and 24

| | |
|-----------------|---|
| End point title | Change From Baseline in BPI-sf Pain Interference With Enjoyment of Life at Weeks 2, 4, 8, 16 and 24 |
|-----------------|---|

End point description:

BPI-sf was a self-administered questionnaire used to assess the severity of pain and the impact of pain on daily functions during a 24 hour period prior to evaluation at specified/scheduled time points. Subjects recorded a score from range 0 (dose not interfere) to 10 (completely interfere) on IRT diaries, which best described their pain interference with enjoyment of life in the last 24 hours at specified time points. Higher scores signified more interference. mITT set analyzed. Multiple imputation applied. 99999: summarised data not available. Individual values at wk 2,4,8,16,24 for 10 mg: 0, -3, -5, -5, -2, -6, -2, -2 -2, -1, -2, 0, -8, -3, -5, -2, 0, -2, -1, -5, -2, -8, -3, -5, -3, -1, -3, -5, -2, -3, -5, -3, -4, -6, -3, -3, -6, 4, -4; for 10/20mg: 5,5,6 respectively. 99999=no subjects were analysed. N:subjects evaluable for endpoint. n:subjects evaluable at specified time points.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|-------------------------------------|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 1 | 71 |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Week 2 (n=73, 9, 1, 71) | -0.72 (± 0.38) | 99999 (± 99999) | 99999 (± 99999) | -0.95 (± 0.41) |
| Change at Week 4 (n=73, 9, 1, 71) | -0.86 (± 0.40) | 99999 (± 99999) | 99999 (± 99999) | -1.42 (± 0.41) |
| Change at Week 8 (n=73, 9, 1, 71) | 0.06 (± 0.42) | 99999 (± 99999) | 99999 (± 99999) | -0.80 (± 0.43) |
| Change at Week 16 (n=73, 6, 0, 71) | -0.12 (± 0.45) | 99999 (± 99999) | 99999 (± 99999) | -0.83 (± 0.46) |

| | | | | |
|------------------------------------|---------------------|----------------------|----------------------|---------------------|
| Change at Week 24 (n=73, 6, 0, 71) | -0.46 (\pm 0.47) | 99999 (\pm 99999) | 99999 (\pm 99999) | -0.82 (\pm 0.48) |
|------------------------------------|---------------------|----------------------|----------------------|---------------------|

Statistical analyses

| Statistical analysis title | Placebo vs Tanezumab 20mg |
|---|----------------------------|
| Statistical analysis description: | |
| Change at Week 2: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference with enjoyment of life, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.5654 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.24 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.05 |
| upper limit | 0.57 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.41 |

| Statistical analysis title | Placebo vs Tanezumab 20mg |
|---|---------------------------|
| Statistical analysis description: | |
| Change at Week 4: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference with enjoyment of life, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.1931 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.57 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.42 |
| upper limit | 0.29 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.43 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.064 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.77 |
| upper limit | 0.05 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.46 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.1478 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.69 |
| upper limit | 0.26 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.49 |

| | |
|--|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 24: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference with enjoyment of life, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.4787 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.35 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.34 |
| upper limit | 0.63 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.5 |

Secondary: Change From Baseline in BPI-sf Pain Interference With General Activity at Weeks 2, 4, 8, 16 and 24

| | |
|---|--|
| End point title | Change From Baseline in BPI-sf Pain Interference With General Activity at Weeks 2, 4, 8, 16 and 24 |
| End point description: | |
| BPI-sf was a self-administered questionnaire used to assess the severity of pain and the impact of pain on daily functions during a 24 hour period prior to evaluation at specified/scheduled time points. Subjects recorded a score from range 0 (dose not interfere) to 10 (completely interfere) on IRT diaries, which best described their pain interference with general activity in the last 24 hours at specified time points. Higher scores signified more interference. mITT set analysed. Multiple imputation applied. 99999: summarised data not available. Individual values at wk 2,4,8,16,24 for 10 mg: 0, 2, -6, -4, -4, -5, -2, -4,0, -1, -1, -1, -6, -4, -4, 0, -3,-2, -2, 0, -4, -7, -5, -5, -3, -1,-2, -5, -1, -5, -5, -2,-3, -6, 2, -5, -4, 5,-3; for 10/20mg: 3,2,1 respectively. 99999=no subjects were analysed. N:subjects evaluable for endpoint. n:subjects evaluable at specified time points. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 2, 4, 8, 16 and 24 | |

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|-------------------------------------|---------------------|----------------------|----------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 1 | 71 |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Week 2 (n=73, 9, 1, 71) | -0.89 (\pm 0.35) | 99999 (\pm 99999) | 99999 (\pm 99999) | -1.18 (\pm 0.39) |
| Change at Week 4 (n=73, 9, 1, 71) | -0.79 (\pm 0.38) | 99999 (\pm 99999) | 99999 (\pm 99999) | -1.50 (\pm 0.39) |
| Change at Week 8 (n=73, 9, 1, 71) | -0.45 (\pm 0.41) | 99999 (\pm 99999) | 99999 (\pm 99999) | -1.58 (\pm 0.43) |
| Change at Week 16 (n=73, 6, 0, 71) | -0.47 (\pm 0.47) | 99999 (\pm 99999) | 99999 (\pm 99999) | -1.17 (\pm 0.48) |
| Change at Week 24 (n=73, 6, 0, 71) | -0.54 (\pm 0.45) | 99999 (\pm 99999) | 99999 (\pm 99999) | -1.01 (\pm 0.44) |

Statistical analyses

| Statistical analysis title | Placebo vs Tanezumab 20mg |
|--|----------------------------|
| Statistical analysis description: | |
| Change at Week 2: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference with general activity, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.4629 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.28 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.05 |
| upper limit | 0.48 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.39 |

| Statistical analysis title | Placebo vs Tanezumab 20mg |
|--|---------------------------|
| Statistical analysis description: | |
| Change at Week 4: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference with general activity, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0886 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.53 |
| upper limit | 0.11 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.41 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0145 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -1.13 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.04 |
| upper limit | -0.23 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.46 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

| | |
|---|----------------------------|
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.1681 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.71 |
| upper limit | 0.3 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.51 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.3249 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.48 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.43 |
| upper limit | 0.48 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.48 |

Secondary: Change From Baseline in BPI-sf Pain Interference With Walking Ability at Weeks 2, 4, 8, 16 and 24

| | |
|-----------------|---|
| End point title | Change From Baseline in BPI-sf Pain Interference With Walking Ability at Weeks 2, 4, 8, 16 and 24 |
|-----------------|---|

End point description:

BPI-sf was a self-administered questionnaire used to assess the severity of pain and the impact of pain on daily functions during a 24 hour period prior to evaluation at specified/scheduled time points. Subjects recorded a score from range 0 (dose not interfere) to 10 (completely interfere) on IRT diaries, which best described their pain interference with walking ability in the last 24 hours at specified time points. Higher scores signified more interference. mITT set analysed. Multiple imputation applied. 99999: summarised data not available. Individual values at wk 2,4,8,16,24 for 10 mg: 1, 2, -5, -2, -6, -4, -1, 0,-5, 0, 3, 0, -5, -5, -4, -2, 0,-2, 0, 1, 4, -6, -7, -5, -1, 4,-3, -4, 0, -7, -6, 2,-4, -5, 2, -7, -5, 7,-4; for 10/20mg: 2,1,2 respectively. 99999=no subjects were analysed. N:subjects evaluable for

endpoint. n:subjects evaluable at specified time points.

| | |
|------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 2, 4, 8, 16 and 24 | |

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|-------------------------------------|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 1 | 71 |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Week 2 (n=73, 9, 1, 71) | -0.58 (± 0.35) | 99999 (± 99999) | 99999 (± 99999) | -0.77 (± 0.37) |
| Change at Week 4 (n=73, 9, 1, 71) | -0.76 (± 0.37) | 99999 (± 99999) | 99999 (± 99999) | -1.11 (± 0.38) |
| Change at Week 8 (n=73, 9, 1, 71) | -0.33 (± 0.42) | 99999 (± 99999) | 99999 (± 99999) | -1.23 (± 0.44) |
| Change at Week 16 (n=73, 6, 0, 71) | -0.28 (± 0.46) | 99999 (± 99999) | 99999 (± 99999) | -0.66 (± 0.48) |
| Change at Week 24 (n=73, 6, 0, 71) | -0.38 (± 0.39) | 99999 (± 99999) | 99999 (± 99999) | -0.48 (± 0.39) |

Statistical analyses

| | |
|---|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 2: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference with walking ability, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.6289 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.19 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.95 |
| upper limit | 0.58 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.39 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.3865 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.35 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.14 |
| upper limit | 0.45 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.4 |

Statistical analysis title

Placebo vs Tanezumab 20mg

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0512 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.8 |
| upper limit | 0 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.46 |

Statistical analysis title

Placebo vs Tanezumab 20mg

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.4272 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.38 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.34 |
| upper limit | 0.57 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.48 |

| | |
|--|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 24: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference with walking ability, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.8107 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.93 |
| upper limit | 0.73 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.42 |

Secondary: Change From Baseline in BPI-sf Pain Interference With Sleep at Weeks 2, 4, 8, 16 and 24

| | |
|-----------------|---|
| End point title | Change From Baseline in BPI-sf Pain Interference With Sleep at Weeks 2, 4, 8, 16 and 24 |
|-----------------|---|

End point description:

BPI-sf was a self-administered questionnaire used to assess the severity of pain and the impact of pain on daily functions during a 24 hour period prior to evaluation at specified/scheduled time points. Subjects recorded a score from range 0 (dose not interfere) to 10 (completely interfere) on IRT diaries, which best described their pain interference with sleep in the last 24 hours at specified time points. Higher scores signified more interference. mITT set analysed. Multiple imputation applied. 99999: summarised data not available. Individual values at wk 2,4,8,16,24 for 10 mg: -1, -1, -3, -6, -1, 0, 0,

-2,-2, 0, 1, 1, -6, -3, 1, -1, -3,-2, 0, -2, -1, -6, -3, 0, 0, -2,-2, -5, -2, -3, -1, -4,-4, -2, -1, -3, 1, 1,-3;
for 10/20mg: 4,3,4 respectively. 99999=no subjects were analysed. N:subjects evaluable for endpoint.
n:subjects evaluable at specified time points.

| | |
|------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 2, 4, 8, 16 and 24 | |

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|-------------------------------------|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 1 | 71 |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Week 2 (n=73,9,1,71) | -0.69 (± 0.43) | 99999 (± 99999) | 99999 (± 99999) | -0.86 (± 0.45) |
| Change at Week 4 (n=73,9,1,71) | -0.81 (± 0.40) | 99999 (± 99999) | 99999 (± 99999) | -1.69 (± 0.41) |
| Change at Week 8 (n=73,9,1,71) | -0.43 (± 0.42) | 99999 (± 99999) | 99999 (± 99999) | -1.15 (± 0.43) |
| Change at Week 16 (n=73, 6, 0, 71) | -0.33 (± 0.46) | 99999 (± 99999) | 99999 (± 99999) | -0.75 (± 0.46) |
| Change at Week 24 (n=73, 6, 0, 71) | -0.18 (± 0.46) | 99999 (± 99999) | 99999 (± 99999) | -0.70 (± 0.46) |

Statistical analyses

| | |
|----------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|----------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.7082 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.07 |
| upper limit | 0.73 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.45 |

| | |
|---|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 4: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference with sleep, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.045 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.87 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.73 |
| upper limit | -0.02 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.43 |

| | |
|---|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 8: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference with sleep, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.1176 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.62 |
| upper limit | 0.18 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.46 |

| | |
|---|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 16: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, | |

and baseline bpi-sf pain interference with sleep, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates.

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.3959 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.41 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.38 |
| upper limit | 0.55 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.49 |

| | |
|--|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 24: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference with sleep, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.2945 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.52 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.49 |
| upper limit | 0.46 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.49 |

Secondary: Change From Baseline in BPI-sf Pain Interference With Normal Work at Weeks 2, 4, 8, 16 and 24

| | |
|-----------------|---|
| End point title | Change From Baseline in BPI-sf Pain Interference With Normal Work at Weeks 2, 4, 8, 16 and 24 |
|-----------------|---|

End point description:

BPI-sf was a self-administered questionnaire used to assess the severity of pain and the impact of pain on daily functions during a 24 hour period prior to evaluation at specified/scheduled time points. Subjects recorded a score from range 0 (dose not interfere) to 10 (completely interfere) on IRT diaries, which best described their pain interference with normal work in the last 24 hours at specified time

points. Higher scores signified more interference. mITT set analysed. Multiple imputation applied. 99999: summarised data not available. Individual values at wk 2,4,8,16,24 for 10 mg: 1, 1, -8, 0, -5, -4, -2, -2,-5, 0, 0, -2, -1, -5, -4, -2, -3, -2, 0, -1, 2, -4, -7, -4, -2, -1,-3, -4, 0, -3, -4, -3, -4, -3, 0, -7, -5, 4,-4; for 10/20mg: 1,1,2 respectively. 99999=no subjects were analysed. N:subjects evaluable for endpoint. n:subjects evaluable at specified time points.

| | |
|------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 2, 4, 8, 16 and 24 | |

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|-------------------------------------|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 1 | 71 |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Week 2 (n=73,9,1,71) | -0.67 (± 0.38) | 99999 (± 99999) | 99999 (± 99999) | -0.90 (± 0.41) |
| Change at Week 4 (n=73,9,1,71) | -0.76 (± 0.36) | 99999 (± 99999) | 99999 (± 99999) | -1.29 (± 0.36) |
| Change at Week 8 (n=73,9,1,71) | -0.32 (± 0.44) | 99999 (± 99999) | 99999 (± 99999) | -0.93 (± 0.45) |
| Change at Week 16 (n=73,6,0,71) | -0.24 (± 0.48) | 99999 (± 99999) | 99999 (± 99999) | -0.69 (± 0.48) |
| Change at Week 24 (n=73,6,0,71) | -0.39 (± 0.43) | 99999 (± 99999) | 99999 (± 99999) | -0.77 (± 0.44) |

Statistical analyses

| | |
|---|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 2: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference with normal work, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.5771 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.23 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.06 |
| upper limit | 0.59 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.42 |

| | |
|---|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 4: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference with normal work, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.1692 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.53 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 0.23 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.39 |

| | |
|---|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 8: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference with normal work, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.2031 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.62 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.57 |
| upper limit | 0.34 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.48 |

| | |
|--|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 16: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference with normal work, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.3716 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.44 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.42 |
| upper limit | 0.53 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.49 |

| | |
|--|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 24: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference with normal work, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.4111 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.39 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.31 |
| upper limit | 0.54 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.47 |

Secondary: Change From Baseline in BPI-sf Pain Interference With Mood at Weeks 2, 4, 8, 16 and 24

| | |
|-----------------|--|
| End point title | Change From Baseline in BPI-sf Pain Interference With Mood at Weeks 2, 4, 8, 16 and 24 |
|-----------------|--|

End point description:

BPI-sf was a self-administered questionnaire used to assess the severity of pain and the impact of pain on daily functions during a 24 hour period prior to evaluation at specified/scheduled time points. Subjects recorded a score from range 0 (dose not interfere) to 10 (completely interfere) on IRT diaries, which best described their pain interference with mood in the last 24 hours at specified time points. Higher scores signified more interference. mITT set analysed. Multiple imputation applied. 99999: summarised data not available. Individual values at wk 2,4,8,16,24 for 10 mg: 0, 1, -4, -2, -2, -7, -1, -4, -2, 1, -1, 1, -7, -3, -6, 0, -4, -2, -1, -1, -1, -8, -3, -7, -1, -2, -3, -5, 1, -1, -6, -3, -4, -4, 0, -3, -6, 4, -3; for 10/20mg: 3,3,3 respectively. 99999=no subjects were analysed. N:subjects evaluable for endpoint. n:subjects evaluable at specified time points.

| | |
|------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 2, 4, 8, 16 and 24 | |

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|-------------------------------------|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 1 | 71 |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Week 2 (n=73, 9,1,71) | -0.93 (± 0.38) | 99999 (± 99999) | 99999 (± 99999) | -1.20 (± 0.41) |
| Change at Week 4 (n=73, 9,1,71) | -1.14 (± 0.37) | 99999 (± 99999) | 99999 (± 99999) | -1.71 (± 0.38) |
| Change at Week 8 (n=73, 9,1,71) | -0.69 (± 0.42) | 99999 (± 99999) | 99999 (± 99999) | -1.44 (± 0.42) |
| Change at Week 16 (n=73, 6, 0, 71) | -0.56 (± 0.47) | 99999 (± 99999) | 99999 (± 99999) | -1.24 (± 0.48) |
| Change at Week 24 (n=73, 6, 0, 71) | -0.65 (± 0.48) | 99999 (± 99999) | 99999 (± 99999) | -1.23 (± 0.47) |

Statistical analyses

| | |
|----------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|----------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.5266 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.27 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 0.57 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.42 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.1599 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.57 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.37 |
| upper limit | 0.23 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.4 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0966 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.64 |
| upper limit | 0.14 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.45 |

| | |
|---|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 16: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference with mood, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.184 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.68 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.68 |
| upper limit | 0.33 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.51 |

| | |
|---|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 24: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference with mood, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.2494 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.58 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.57 |
| upper limit | 0.41 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.5 |

Secondary: Change From Baseline in BPI-sf Pain Interference With Relations With Other People at Weeks 2, 4, 8, 16 and 24

| | |
|---|---|
| End point title | Change From Baseline in BPI-sf Pain Interference With Relations With Other People at Weeks 2, 4, 8, 16 and 24 |
| End point description: | |
| BPI-sf was a self-administered questionnaire used to assess the severity of pain and the impact of pain on daily functions during a 24 hour period prior to evaluation at specified/scheduled time points. Subjects recorded a score from range 0 (dose not interfere) to 10 (completely interfere) on IRT diaries, which best described their pain interference with relations with other people in the last 24 hours at specified time points. Higher scores signified more interference. mITT set analysed. Multiple imputation applied. 99999: summarised data not available. Individual values at wk 2,4,8,16,24 for 10 mg: 2, -1, -4, -5, -7, -6, -2, -4,-5, 0, -2, -1, -8, -7, -6, -2, -4,-2, -1, -3, -3, -9, -7, -6, -1, 0,-3, -3, -1, -7, -5, -2,-4, -5, -3, -7, -6, 5,-4; for 10/20mg: 8,7,9 respectively. 99999=no subjects were analysed. N:subjects evaluable for endpoint. n:subjects evaluable at specified time points. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 2, 4, 8, 16 and 24 | |

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|-------------------------------------|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 1 | 71 |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Week 2 (n=73, 9, 1, 71) | -0.93 (± 0.36) | 99999 (± 99999) | 99999 (± 99999) | -0.75 (± 0.39) |
| Change at Week 4 (n=73, 9, 1, 71) | -1.05 (± 0.41) | 99999 (± 99999) | 99999 (± 99999) | -1.24 (± 0.41) |
| Change at Week 8 (n=73, 9, 1, 71) | -0.66 (± 0.42) | 99999 (± 99999) | 99999 (± 99999) | -1.27 (± 0.42) |
| Change at Week 16 (n=73, 6, 0, 71) | -0.50 (± 0.46) | 99999 (± 99999) | 99999 (± 99999) | -1.12 (± 0.46) |
| Change at Week 24 (n=73, 6, 0, 71) | -0.78 (± 0.40) | 99999 (± 99999) | 99999 (± 99999) | -1.00 (± 0.41) |

Statistical analyses

| | |
|---|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 2: ANCOVA model for imputed datasets includes treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference with relations with other people, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.6573 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | 0.18 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.62 |
| upper limit | 0.98 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.4 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.6511 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.05 |
| upper limit | 0.66 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.43 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.1896 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.6 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.51 |
| upper limit | 0.3 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.46 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.2107 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.62 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.6 |
| upper limit | 0.36 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.49 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.6198 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.21 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.07 |
| upper limit | 0.64 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.43 |

Secondary: Change From Baseline in BPI-sf Pain Interference Index at Weeks 2, 4, 8, 16 and 24

| | |
|---|--|
| End point title | Change From Baseline in BPI-sf Pain Interference Index at Weeks 2, 4, 8, 16 and 24 |
| End point description: | |
| BPI-sf: self-administered questionnaire to assess severity and impact of pain on daily functions during 24 hour period prior to evaluation at specified time points. Pain interference index=mean of 7 BPI-sf pain interference items: pain interference with general activity; mood; walking ability; normal work; relations with other people; sleep and enjoyment of life. Score range: 7 items=0 to 10 (no to complete interference), higher scores=more interference in daily activities due to pain. Overall score range: pain interference index=0 to 10 (no to complete interference). Higher scores=more interference. 99999=summarised data not available. Individual values at wk2,4,8,16,24 for 10mg: 0.42, 0.14, -5, -3.42, -3.85, -4.57, -1.42, -2.57, -3, -0.14, -0.28, -0.28, -5.85, -4.28, -4, -1.28, -2.42, -2, -0.71, -1.57, -0.71, -6.85, -5, -4.57, -1.57, -0.42, -2.71, -4.42, -0.71, -4.14, -4.57, -2.14, -3.85, -4.42, -0.71, -4.14, -4.42, -0.42, -5, -4.42, 4.28, -3.57; 10/20mg: 3.71, 3.14, 3.85. 'N': subjects evaluable for this end point, | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 2, 4, 8, 16 and 24 | |

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|-------------------------------------|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 1 | 71 |
| Units: Units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Week 2 (n=73,9,1,71) | -0.77 (± 0.31) | 99999 (± 99999) | 99999 (± 99999) | -0.96 (± 0.34) |
| Change at Week 4 (n=73,9,1,71) | -0.88 (± 0.33) | 99999 (± 99999) | 99999 (± 99999) | -1.42 (± 0.34) |
| Change at Week 8 (n=73,9,1,71) | -0.41 (± 0.37) | 99999 (± 99999) | 99999 (± 99999) | -1.21 (± 0.38) |
| Change at Week 16 (n=73,6,1,71) | -0.34 (± 0.42) | 99999 (± 99999) | 99999 (± 99999) | -0.93 (± 0.44) |
| Change at Week 24 (n=73,6,1,71) | -0.49 (± 0.40) | 99999 (± 99999) | 99999 (± 99999) | -0.85 (± 0.41) |

Statistical analyses

| | |
|---|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Change at Week 2: ANCOVA model for imputed datasets includes treatment, region, and randomisation | |

stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and baseline bpi-sf pain interference index, baseline average pain intensity at the index bone metastasis cancer pain site, and baseline opioid dose as covariates.

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.5842 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.19 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.87 |
| upper limit | 0.49 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.34 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.122 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.55 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.24 |
| upper limit | 0.15 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.35 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

| | |
|---|----------------------------|
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0462 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.58 |
| upper limit | -0.01 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.4 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.1922 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.59 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.48 |
| upper limit | 0.3 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.45 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

| | |
|---|----------------------------|
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.38 |
| Method | ANCOVA |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.37 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.19 |
| upper limit | 0.46 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.42 |

Secondary: Number of Subjects With Responses to Mobility Dimension of EuroQol 5 Dimension 5 Level (EQ-5D-5L) Scale at Baseline, Weeks 8, 16 and 24

| | |
|-----------------|---|
| End point title | Number of Subjects With Responses to Mobility Dimension of EuroQol 5 Dimension 5 Level (EQ-5D-5L) Scale at Baseline, Weeks 8, 16 and 24 |
|-----------------|---|

End point description:

EQ-5D-5L is a standardised subject completed questionnaire that measures health-related quality of life 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. Each dimension has 5 levels: 1= no problems, 2= slight problems, 3= moderate problems, 4= severe problems, and 5= extreme problems. Higher scores indicated greater levels of problems across each of the five dimensions. mITT analysis set was analysed. Multiple imputation method was applied. Here, 'N': subjects evaluable for this end point, 'n': subjects evaluable at specified time points.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 8, 16 and 24

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|--|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 1 | 71 |
| Units: Subjects | | | | |
| Baseline I have no problems walking(n=73,9,1,71) | 7 | 1 | 0 | 8 |
| Week 8 I have no problems walking (n=54,9,1,60) | 10 | 3 | 0 | 8 |
| Week 16 I have no problems walking (n=40,6,0,47) | 10 | 2 | 0 | 10 |
| Week 24 I have no problems walking (n=34,6,0,37) | 8 | 1 | 0 | 9 |
| Baseline slight problems walking (n=73,9,1,71) | 30 | 4 | 0 | 26 |
| Week 8 I have slight problems walking(n=54,9,1,60) | 24 | 1 | 0 | 33 |

| | | | | |
|--|----|---|---|----|
| Week 16 have slight problems walking(n=40,6,0,47) | 20 | 3 | 0 | 24 |
| Week 24 have slight problems walking(n=34,6,0,37) | 20 | 3 | 0 | 18 |
| Baseline moderate problems walking (n=73,9,1,71) | 30 | 4 | 1 | 25 |
| Week 8 have moderate problems walking(n=54,9,1,60) | 13 | 3 | 0 | 12 |
| Week16 have moderate problems walking(n=40,6,0,47) | 9 | 1 | 0 | 8 |
| Week24 have moderate problems walking(n=34,6,0,37) | 5 | 0 | 0 | 10 |
| Baseline have severe problems walking n=73,9,1,71 | 6 | 0 | 0 | 10 |
| Week 8 I have severe problems walking(n=54,9,1,60) | 5 | 1 | 1 | 5 |
| Week 16 have severe problems walking (n=40,6,0,47) | 1 | 0 | 0 | 4 |
| Week 24 have severe problems walking (n=34,6,0,37) | 1 | 2 | 0 | 0 |
| Baseline I am unable to walk (n=73,9,1,71) | 0 | 0 | 0 | 2 |
| Week 8 I am unable to walk(n=54,9,1,60) | 2 | 1 | 0 | 2 |
| Week 16 I am unable to walk(n=40,6,0,47) | 0 | 0 | 0 | 1 |
| Week 24 I am unable to walk(n=34,6,0,37) | 0 | 0 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Responses to Self-Care Dimension of EQ-5D-5L Scale at Baseline, Weeks 8, 16 and 24

| | |
|-----------------|--|
| End point title | Number of Subjects With Responses to Self-Care Dimension of EQ-5D-5L Scale at Baseline, Weeks 8, 16 and 24 |
|-----------------|--|

End point description:

EQ-5D-5L is a standardised subject completed questionnaire that measures health-related quality of life 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 VAS. EQ-5D health state profile is comprised of 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 levels: 1= no problems, 2= slight problems, 3= moderate problems, 4= severe problems, and 5= extreme problems. Higher scores indicated greater levels of problems across each of the five dimensions. mITT analysis set was analysed. Multiple imputation method was applied. Here, 'N': subjects evaluable for this end point, 'n': subjects evaluable at specified time points.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 8, 16 and 24

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|--|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 1 | 71 |
| Units: Subjects | | | | |
| Baseline no problems wash,dress (n=73,9,1,72) | 27 | 4 | 0 | 28 |
| Week8 no problems wash,dress myself (n=54,9,1,60) | 21 | 5 | 0 | 35 |
| Week16 no problems wash,dress myself (n=40,6,0,47) | 23 | 4 | 0 | 30 |
| Week24 no problems wash,dress myself(n=34,6,0,37) | 23 | 4 | 0 | 23 |
| Baseline slight problem wash,dress (n=73,9,1,72) | 25 | 4 | 0 | 22 |
| Week8 slight problems wash or dress(n=54,9,1,60) | 19 | 1 | 0 | 13 |
| Week16 slight problems wash or dress(n=40,6,0,47) | 8 | 1 | 0 | 9 |
| Week24 slight problems wash or dress(n=34,6,0,37) | 6 | 0 | 0 | 10 |
| Baseline moderate problems wash,dress(n=73,9,1,72) | 18 | 1 | 1 | 16 |
| Week8 moderate problems wash or dress n=54,9,1,60 | 9 | 1 | 0 | 7 |
| Week16 moderate problems wash or dress n=40,6,0,47 | 8 | 1 | 0 | 7 |
| Week24 moderate problems wash or dress n=34,6,0,37 | 4 | 0 | 0 | 4 |
| Baseline severe problems wash or dress n=73,9,1,72 | 3 | 0 | 0 | 4 |
| Week 8 severe problems wash or dress (n=54,9,1,60) | 4 | 1 | 1 | 3 |
| Week16 severe problems wash or dress (n=40,6,0,47) | 1 | 0 | 0 | 1 |
| Week24 severe problems wash or dress (n=34,6,0,37) | 1 | 1 | 0 | 0 |
| Baseline unable: wash or dress myself n=73,9,1,72 | 0 | 0 | 0 | 1 |
| Week8 unable to wash or dress myself(n=54,9,1,60) | 1 | 1 | 0 | 2 |
| Week16 unable to wash or dress myself(n=40,6,0,47) | 0 | 0 | 0 | 0 |
| Week24 unable to wash or dress myself(n=34,6,0,37) | 0 | 1 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Responses to Usual Activities Dimension of EQ-5D-5L Scale at Baseline, Weeks 8, 16 and 24

| | |
|-----------------|---|
| End point title | Number of Subjects With Responses to Usual Activities Dimension of EQ-5D-5L Scale at Baseline, Weeks 8, 16 and 24 |
|-----------------|---|

End point description:

EQ-5D-5L is a standardised subject completed questionnaire that measures health-related quality of life 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 VAS. EQ-5D health state profile is comprised of 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 levels: 1= no problems, 2= slight problems, 3= moderate problems, 4= severe problems, and 5= extreme problems. Higher scores indicated greater levels of problems across each of the five dimensions. mITT analysis set was analysed. Multiple imputation method was applied. Here, 'N': subjects evaluable for this end point, 'n': subjects evaluable at specified time points.

| | |
|------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 8, 16 and 24 | |

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|---|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 1 | 71 |
| Units: Subjects | | | | |
| Baseline no problem in usual activity n=73,9,1,71 | 7 | 1 | 0 | 9 |
| Week8 no problem in usual activity(n=54,9,1,60) | 11 | 2 | 0 | 14 |
| Week16 no problem in usual activity(n=40,6,0,47) | 15 | 1 | 0 | 15 |
| Week 24 no problem in usual activity(n=34,6,0,37) | 15 | 2 | 0 | 9 |
| Baseline slight problem:usual activity n=73,9,1,71 | 28 | 5 | 0 | 33 |
| Week8 slight problem:usual activity(n=54,9,1,60) | 21 | 3 | 0 | 29 |
| Week16 slight problem:usual activity(n=40,6,0,47) | 12 | 4 | 0 | 23 |
| Week24 slight problem:usual activity(n=34,6,0,37) | 14 | 2 | 0 | 21 |
| Baseline moderate problem (n=73,9,1,71) | 31 | 2 | 0 | 21 |
| Week8 moderate problem:usual activity(n=54,9,1,60) | 14 | 2 | 0 | 12 |
| Week16 moderate problem:usual activity n=40,6,0,47 | 10 | 1 | 0 | 7 |
| Week24 moderate problem:usual activity n=34,6,0,37 | 4 | 0 | 0 | 6 |
| Baseline severe problem:usual activity n=73,9,1,71 | 7 | 1 | 1 | 6 |
| Week8 severe problems:usual activity(n=54,9,1,60) | 6 | 2 | 0 | 2 |
| Week16 severe problems:usual activity(n=40,6,0,47) | 3 | 0 | 0 | 1 |
| Week24 severe problem:usual activity(n=34,6,0,37) | 1 | 1 | 0 | 1 |
| Baseline unable to do usual activity(n=73,9,1,71) | 0 | 0 | 0 | 2 |
| Week8 unable to do my usual activity(n=54,9,1,60) | 2 | 0 | 1 | 3 |
| Week16 unable to do my usual activity(n=40,6,0,47) | 0 | 0 | 0 | 1 |
| Week24 unable to do my usual activity(n=34,6,0,37) | 0 | 1 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Responses to Pain/Discomfort Dimension of EQ-5D-5L Scale at Baseline, Weeks 8, 16 and 24

| | |
|-----------------|--|
| End point title | Number of Subjects With Responses to Pain/Discomfort Dimension of EQ-5D-5L Scale at Baseline, Weeks 8, 16 and 24 |
|-----------------|--|

End point description:

EQ-5D-5L is a standardised subject completed questionnaire that measures health-related quality of life 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 VAS. EQ-5D health state profile is comprised of 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 levels: 1= no problems, 2= slight problems, 3= moderate problems, 4= severe problems, and 5= extreme problems. Higher scores indicated greater levels of problems across each of the five dimensions. mITT analysis set was analysed. Multiple imputation method was applied. Here, 'N': subjects evaluable for this end point, 'n': subjects evaluable at specified time points.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 8, 16 and 24

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|--|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 1 | 71 |
| Units: Subjects | | | | |
| Baseline I have no pain or discomfort(n=73,9,1,71) | 0 | 0 | 0 | 0 |
| Week 8 I have no pain or discomfort (n=54,9,1,60) | 3 | 2 | 0 | 5 |
| Week 16 I have no pain or discomfort (n=40,6,0,47) | 1 | 1 | 0 | 6 |
| Week 24 I have no pain or discomfort (n=34,6,0,37) | 1 | 1 | 0 | 6 |
| Baseline slight pain or discomfort (n=73,9,1,71) | 10 | 1 | 0 | 9 |
| Week8 have slight pain or discomfort(n=54,9,1,60) | 17 | 3 | 0 | 32 |
| Week16 have slight pain or discomfort(n=40,6,0,47) | 16 | 4 | 0 | 26 |
| Week24 have slight pain or discomfort(n=34,6,0,37) | 18 | 3 | 0 | 17 |
| Baseline moderate pain or discomfort(n=73,9,1,71) | 40 | 5 | 1 | 41 |
| Week8 moderate pain or discomfort(n=54,9,1,60) | 26 | 4 | 0 | 17 |
| Week16 moderate pain or discomfort(n=40,6,0,47) | 19 | 1 | 0 | 14 |

| | | | | |
|--|----|---|---|----|
| Week24 moderate pain or discomfort(n=34,6,0,37) | 12 | 0 | 0 | 11 |
| Baseline severe pain or discomfort(n=73,9,1,71) | 23 | 3 | 0 | 20 |
| Week8 severe pain or discomfort(n=54,9,1,60) | 7 | 0 | 1 | 6 |
| Week16 severe pain or discomfort(n=40,6,0,47) | 4 | 0 | 0 | 1 |
| Week 24 severe pain or discomfort(n=34,6,0,37) | 3 | 1 | 0 | 3 |
| Baseline extreme pain or discomfort(n=73,9,1,71) | 0 | 0 | 0 | 1 |
| Week8 have extreme pain or discomfort(n=54,9,1,60) | 1 | 0 | 0 | 0 |
| Week16 have extreme pain or discomfort n=40,6,0,47 | 0 | 0 | 0 | 0 |
| Week24 have extreme pain or discomfort n=34,6,0,37 | 0 | 1 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Responses to Anxiety/Depression Dimension of EQ-5D-5L Scale at Baseline, Weeks 8, 16 and 24

| | |
|-----------------|---|
| End point title | Number of Subjects With Responses to Anxiety/Depression Dimension of EQ-5D-5L Scale at Baseline, Weeks 8, 16 and 24 |
|-----------------|---|

End point description:

EQ-5D-5L is a standardised subject completed questionnaire that measures health-related quality of life 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 VAS. EQ-5D health state profile is comprised of 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 levels: 1= no problems, 2= slight problems, 3= moderate problems, 4= severe problems, and 5= extreme problems. Higher scores indicated greater levels of problems across each of the five dimensions. mITT analysis set was analysed. Multiple imputation method was applied. Here, 'N': subjects evaluable for this end point, 'n': subjects evaluable at specified time points.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 8, 16 and 24

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|---|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 1 | 71 |
| Units: Subjects | | | | |
| Baseline I am not anxious or depressed n=73,9,1,71 | 17 | 1 | 0 | 23 |
| Week 8 I am not anxious or depressed (n=54,9,1,60) | 24 | 2 | 0 | 29 |
| Week16 I am not anxious or depressed (n=40,6,0,47) | 18 | 3 | 0 | 25 |
| Week24 I am not anxious or depressed (n=34,6,0,37) | 19 | 4 | 0 | 23 |

| | | | | |
|---|----|---|---|----|
| Baseline slightly anxious or depressed n=73,9,1,71 | 28 | 5 | 1 | 23 |
| Week8 slightly anxious or depressed (n=54,9,1,60) | 14 | 4 | 0 | 21 |
| Week16 slightly anxious or depressed(n=40,6,0,47) | 12 | 2 | 0 | 15 |
| Week 24 slightly anxious or depressed(34,6,0,37) | 11 | 0 | 0 | 8 |
| Baseline moderate anxious or depressed n=73,9,1,71 | 20 | 2 | 0 | 19 |
| Week8 moderately anxious or depressed(n=54,9,1,60) | 12 | 2 | 1 | 6 |
| Week16 moderately anxious or depressed n=40,6,0,47 | 9 | 1 | 0 | 5 |
| Week24 moderately anxious or depressed n=34,6,0,37 | 4 | 1 | 0 | 5 |
| Baseline severely anxious or depressed n=73,9,1,71 | 8 | 1 | 0 | 5 |
| Week8 severely anxious or depressed(n=54,9,1,60) | 4 | 1 | 0 | 4 |
| Week16 severely anxious or depressed(n=40,6,0,47) | 1 | 0 | 0 | 2 |
| Week24 severely anxious or depressed(n=34,6,0,37) | 0 | 0 | 0 | 1 |
| Baseline extreme anxious or depressed n=73,9,1,71 | 0 | 0 | 0 | 1 |
| Week8 extremely anxious or depressed(n=54,9,1,60) | 0 | 0 | 0 | 0 |
| Week16 extremely anxious or depressed(n=40,6,0,47) | 0 | 0 | 0 | 0 |
| Week24 extremely anxious or depressed(n=34,6,0,37) | 0 | 1 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: EQ-5D-5L Scale Index Value at Baseline, Weeks 8, 16 and 24

| | |
|-----------------|--|
| End point title | EQ-5D-5L Scale Index Value at Baseline, Weeks 8, 16 and 24 |
|-----------------|--|

End point description:

EQ-5D health state profile:5 dimensions-mobility, self-care, usual activities, pain/discomfort, anxiety/depression. 5 levels for each:1=no problems,2=slight,3=moderate,4=severe,5=extreme. Responses=overall health state/a single utility index value. If response= "no problems" to all 5,health state coded: "11111" with predefined single index value. EuroQol assigned unique predefined utility index value for every health state coded as combination of all 5 domains. Score range: -0.654(minimum score)- 1(maximum score).Higher(positive) scores=better health state. mITT analysis set analysed. Multiple imputation applied. 99999:summarised data not available.Individual values at wk 8,16,24 for 10mg: 0.41,0.14,0.26,0.62,0.65,0.65,0.54, 0.56,0.77,0.63,0.41, 0.09,0.19,0.85,0.55,0.68,0.79,1,0.68,0.52,0.91,0.73,0.59,0.84,0.73,0.15,0.88,0.73,-0.37,0.84;for 10/20mg: 0.423,0.04 respectively. 99999=no subjects analysed. N:subjects evaluable for endpoint. n:subjects evaluable at specified time points.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 8, 16 and 24

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|--------------------------------------|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 1 | 71 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=73,9,1,71) | 0.51 (± 0.19) | 99999 (± 99999) | 99999 (± 99999) | 0.51 (± 0.24) |
| Week 8 (n=54,9,1,60) | 0.56 (± 0.26) | 99999 (± 99999) | 99999 (± 99999) | 0.61 (± 0.25) |
| Week 16 (n=40,6,0,47) | 0.63 (± 0.16) | 99999 (± 99999) | 99999 (± 99999) | 0.67 (± 0.20) |
| Week 24 (n=34,6,0,37) | 0.67 (± 0.13) | 99999 (± 99999) | 99999 (± 99999) | 0.69 (± 0.18) |

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|--------------------------------------|-------------------|-----------------|--------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 1 | 72 |
| Units: mg of MED | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 1 (n=72,9,1,69) | 183.94 (± 275.05) | 99999 (± 99999) | 99999 (± 99999) | 186.86 (± 351.83) |
| Week 2 (n=73,9,1,69) | 177.98 (± 270.67) | 99999 (± 99999) | 99999 (± 99999) | 188.41 (± 356.15) |

| | | | | |
|-----------------------|-------------------|-----------------|-----------------|--------------------|
| Week 4 (n=73,9,1,69) | 177.87 (± 266.93) | 99999 (± 99999) | 99999 (± 99999) | 181.32 (± 349.82) |
| Week 6 (n=73,9,1,70) | 186.20 (± 280.44) | 99999 (± 99999) | 99999 (± 99999) | 173.45 (± 346.27) |
| Week 8 (n=73,9,1,70) | 188.10 (± 281.01) | 99999 (± 99999) | 99999 (± 99999) | 170.31 (± 327.19) |
| Week 12 (n=73,9,1,70) | 187.43 (± 336.74) | 99999 (± 99999) | 99999 (± 99999) | 177.06 (± 332.39) |
| Week 16 (n=73,9,1,70) | 189.62 (± 333.77) | 99999 (± 99999) | 99999 (± 99999) | 173.48 (± 329.17) |
| Week 24 (n=73,9,1,70) | 189.78 (± 353.10) | 99999 (± 99999) | 99999 (± 99999) | 346.95 (± 1537.00) |

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

| | | | | |
|-----------------------|---------------|-----------------|-----------------|---------------|
| Week 24 (n=65,9,1,49) | 0.79 (± 0.93) | 99999 (± 99999) | 99999 (± 99999) | 0.69 (± 0.57) |
|-----------------------|---------------|-----------------|-----------------|---------------|

Statistical analyses

No statistical analyses for this end point

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

| | |
|--|--|
| End point title | Change From Baseline in the Weekly Opioid-Related Symptom Distress Scale (OR-SDS) at Weeks 2, 4, 8, 16, and 24 |
| End point description: OR 12 symptoms(Ss) evaluated. Range:severity(none=0 to very severe=4),distress(none =0 to very much=5);frequency(none =0 to almost constantly =4;subjects reported number of retching/vomiting episodes(none =0, 1-2 episodes =1, 3-4 episodes =2, 5-6 episodes =3, >6 episodes =4).Frequency(F)composite score:mean of F scores from all Ss, 0(none) to 4(almost constantly);Severity(S) composite score:mean of S scores from all 12 Ss, 0(none) to 4(max severity);Distress(D)composite score:mean of D scores from all 12 symptoms,0(none) to 5(max distress).Multi domain avg(MDA):avg of each Ss for F,S,D; 0(none)to 4.34(worse);higher scores=worse condition in all domains.99999=Individual values at wk 2,4,8,16,24 for 10 mg:-1,0,-1,-0.67,-0.6,0.2,-0.25,-0.22,-0.8,0,-0.25,-0.35,-1,0,-0.75,-0.58;10/20 mg: -1.33,-0.83,0.17,-0.67,-1.5,-0.5,0,-0.67,-1,-0.75,0.25,-0.5 respectively.9999=not analysed. N:subjects evaluable for endpoint. n:subjects at | |
| End point type | Secondary |
| End point timeframe: Baseline, Weeks 2, 4, 8, 16, and 24 | |

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

| | | | | |
|--|----------------|-----------------|-----------------|----------------|
| Change at Week 8: D Composite Score (n=73,1,72,2) | 0.03 (± 0.19) | 99999 (± 99999) | 99999 (± 99999) | 0.26 (± 0.20) |
| Change at Week8:MDA Composite Score (n=73,1,72,2) | 0.02 (± 0.13) | 99999 (± 99999) | 99999 (± 99999) | -0.02 (± 0.14) |
| Change at Week 16: F Composite Score (n=73,0,72,1) | 0.08 (± 0.19) | 99999 (± 99999) | 99999 (± 99999) | -0.07 (± 0.22) |
| Change at Week 16: S Composite Score (n=73,0,72,1) | -0.12 (± 0.15) | 99999 (± 99999) | 99999 (± 99999) | 0.08 (± 0.17) |
| Change at Week 16: D Composite Score (n=73,0,72,1) | 0.10 (± 0.20) | 99999 (± 99999) | 99999 (± 99999) | -0.07 (± 0.24) |
| Change at Week16:MDA Composite Score(n=73,0,72,1) | 0.02 (± 0.16) | 99999 (± 99999) | 99999 (± 99999) | -0.04 (± 0.19) |
| Change at Week 24: F Composite Score (n=73,0,72,0) | 0.29 (± 0.21) | 99999 (± 99999) | 99999 (± 99999) | -0.13 (± 0.24) |
| Change at Week 24: S Composite Score (n=73,0,72,0) | -0.01 (± 0.17) | 99999 (± 99999) | 99999 (± 99999) | 0.16 (± 0.18) |
| Change at Week24: D Composite Score (n=73,0,72,0) | 0.33 (± 0.21) | 99999 (± 99999) | 99999 (± 99999) | 0.22 (± 0.23) |
| Change at Week24:MDA Composite Score (n=73,0,72,0) | 0.17 (± 0.18) | 99999 (± 99999) | 99999 (± 99999) | 0.07 (± 0.20) |

Statistical analyses

| | |
|---|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 4 Frequency Composite Score: MMRM model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS frequency scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 145 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.7127 |
| Method | Mixed models analysis |
| Parameter estimate | Difference in LS mean |
| Point estimate | 0.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.28 |
| upper limit | 0.41 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.17 |

| | |
|---|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 2 Frequency Composite Score: Mixed model for repeated measurements (MMRM) model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS frequency scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates. | |

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

| | |
|---|----------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 8 Frequency Composite Score: MMRM model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS frequency scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 145 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.3933 |
| Method | Mixed models analysis |
| Parameter estimate | Difference in LS mean |
| Point estimate | -0.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.57 |
| upper limit | 0.23 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.2 |

| | |
|--|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 16 Frequency Composite Score: MMRM model includes time (study week), treatment, region, and randomisation stratification variables (concomitant anticancer treatment and tumor aggressiveness) as fixed effects, and treatment*time interaction, baseline OR-SDS frequency scores, and baseline average pain intensity at the index bone metastasis cancer pain site as covariates. | |
| Comparison groups | Placebo v Tanezumab 20 mg |

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 145 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.477 |
| Method | Mixed models analysis |
| Parameter estimate | Difference in LS mean |
| Point estimate | 0.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.3 |
| upper limit | 0.64 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.23 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|---|----------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 145 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.7181 |
| Method | Mixed models analysis |
| Parameter estimate | Difference in LS mean |
| Point estimate | 0.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.25 |
| upper limit | 0.37 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.15 |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

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

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

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

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

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

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

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

End point description:

An adverse event (AE) was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. Serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent were events between first dose of study drug and up to 24 weeks post last dose that were absent before treatment or that worsened relative to pretreatment state. AEs included both serious and all non-serious AEs. Subjects were followed up to 24 weeks after study drug last dose. The safety analysis set was defined as all subjects treated with tanezumab or placebo SC, including subjects who received tanezumab 10 mg prior to protocol amendment 3.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Notes:

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Notes:

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

| | | | | |
|--|---|---|---|---|
| Sitting DBP(mmHg) Change ≥ 10 to < 20 | 5 | 2 | 0 | 9 |
| Sitting DBP(mmHg) Change ≥ 20 to < 30 | 2 | 1 | 0 | 1 |

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|---|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 40 | 8 | 0 ^[12] | 44 |
| Units: Subjects | | | | |
| QTCB Interval $450 \leq \text{Value} < 480$ | 2 | 1 | | 6 |
| QTCB Interval $480 \leq \text{Value} < 500$ | 0 | 0 | | 1 |
| QTCF Interval $450 \leq \text{Value} < 480$ | 1 | 0 | | 5 |

Notes:

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

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Confirmed Orthostatic Hypotension

| | |
|-----------------|---|
| End point title | Number of Subjects with Confirmed Orthostatic Hypotension |
|-----------------|---|

End point description:

Orthostatic hypotension was defined as postural change (supine to standing) that met the following criteria: for systolic blood pressure (BP) less than or equal to (\leq) 150 millimeter of mercury (mmHg) (mean supine): reduction in systolic BP ≥ 20 mmHg or reduction in diastolic BP ≥ 10 mmHg at the 1 and/or 3 minute standing BP measurements. For systolic BP greater than ($>$) 150 mmHg (mean supine): reduction in systolic BP ≥ 30 mmHg or reduction in diastolic BP ≥ 15 mmHg at the 1 and/or 3 minute standing BP measurements. If the 1 minute or 3 minute standing BP in a sequence met the orthostatic hypotension criteria, then that sequence was considered positive. If 2 of 2 or 2 of 3 sequences were positive, then orthostatic hypotension was considered confirmed. Safety analysis set: all

subjects treated with tanezumab or placebo SC, including subjects received tanezumab 10 mg prior to protocol amendment 3. N:subjects evaluable for endpoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 1 of dosing up to maximum of Week 48

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

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormal Physical Examination at Screening

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

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Screening (up to 37 days prior to Day 1)

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|-----------------------------|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 72 | 9 | 1 | 72 |
| Units: Subjects | | | | |
| General | 3 | 1 | 0 | 6 |
| Head | 2 | 1 | 0 | 1 |
| Eyes | 4 | 1 | 0 | 1 |
| Ears | 1 | 0 | 0 | 1 |
| Nose | 0 | 0 | 0 | 0 |
| Neck | 2 | 1 | 0 | 2 |
| Thyroid | 2 | 0 | 0 | 0 |
| Lungs | 5 | 1 | 0 | 3 |
| Heart | 2 | 2 | 0 | 3 |
| Abdomen | 2 | 1 | 1 | 5 |
| Extremities | 14 | 0 | 0 | 10 |
| Skin | 15 | 2 | 0 | 10 |
| Throat | 3 | 1 | 0 | 2 |
| Other 1 | 9 | 3 | 0 | 6 |
| Other 2 | 1 | 3 | 0 | 2 |
| Other 3 | 0 | 1 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Joint-related safety events resulting in total joint replacement and/or discontinuation from the study as well as adverse events were reviewed by the External Adjudication Committee to confirm the potential events as adjudicated joint safety event. In this endpoint, number of subjects with any of the joint safety adjudication outcomes of primary osteonecrosis, rapidly progressive osteoarthritis (OA) (type 1 and type 2), subchondral insufficiency fracture (or SPONK), or pathological fracture were reported. Other adjudication outcomes included normal progression of OA and other joint outcome. Safety analysis set

was analysed. N:subjects evaluable for endpoint. n:subjects evaluable at specified assessments. In reporting arm, "Tanezumab10/20 mg" the subject did not have potential joint related safety event for analysis by Adjudication Committee.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| During the study, maximum up to Week 48 | |

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

Notes:

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

Statistical analyses

No statistical analyses for this end point

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

| | |
|---|---|
| End point title | Number of Subjects With At Least 1 Total Joint Replacements (TJR) |
| End point description: | |
| Number of subjects with joint replacement surgery were reported. The safety analysis set included all subjects treated with tanezumab or placebo SC, including subjects who received tanezumab 10 mg prior to protocol amendment 3. | |
| End point type | Secondary |
| End point timeframe: | |
| During the study, maximum up to Week 48 | |

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

Statistical analyses

Secondary: Number of Subjects According to Type of Change From Baseline in Neuropathy Impairment Score (NIS) at Weeks 2, 4, 8, 12, 16, 24 and 40

| | |
|-----------------|---|
| End point title | Number of Subjects According to Type of Change From Baseline in Neuropathy Impairment Score (NIS) at Weeks 2, 4, 8, 12, 16, 24 and 40 |
|-----------------|---|

End point description:

NIS is a standardised instrument used to evaluate subjects for signs of peripheral neuropathy. NIS is the 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. In this outcome measure number of subjects were reported in 3 categories at each specified time points. Categories were: 1) worsened = when change from baseline in NIS score was less than zero; 2) no change; 3) improved = when change from baseline in NIS score was greater than zero. Change from baseline in NIS was analyzed using Cochran-Mantel-Haenszel test. mITT analysis set analysed. LOCF data applied. N:subjects evaluable for endpoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1, before dosing), Weeks 2, 4, 8, 12, 16, 24 and 40

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|---------------------------------|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 66 | 9 | 1 | 67 |
| Units: Subjects | | | | |
| Week 2 Worsened (n=65,9,1,62) | 4 | 2 | 0 | 7 |
| Week 4 Worsened (n=66,9,1,66) | 5 | 2 | 1 | 8 |
| Week 8 Worsened (n=66,9,1,66) | 6 | 2 | 0 | 11 |
| Week 12 Worsened (n=66,9,1,66) | 6 | 2 | 0 | 11 |
| Week 16 Worsened (n=66,9,1,67) | 7 | 3 | 0 | 12 |
| Week 24 Worsened (n=66,9,1,67) | 9 | 3 | 0 | 13 |
| Week 40 Worsened (n=66,9,1,67) | 11 | 2 | 0 | 13 |
| Week 2 No Change (n=65,9,1,62) | 54 | 5 | 1 | 47 |
| Week 4 No Change (n=66,9,1,66) | 50 | 6 | 0 | 47 |
| Week 8 No Change (n=66,9,1,66) | 49 | 5 | 1 | 43 |
| Week 12 No Change (n=66,9,1,66) | 49 | 5 | 1 | 43 |
| Week 16 No Change (n=66,9,1,67) | 51 | 5 | 1 | 43 |
| Week 24 No Change (n=66,9,1,67) | 49 | 5 | 1 | 42 |
| Week 40 No Change (n=66,9,1,67) | 47 | 5 | 1 | 45 |
| Week 2 Improved (n=65,9,1,62) | 7 | 2 | 0 | 8 |
| Week 4 Improved (n=66,9,1,66) | 11 | 1 | 0 | 11 |
| Week 8 Improved (n=66,9,1,66) | 11 | 2 | 0 | 12 |
| Week 12 Improved (n=66,9,1,66) | 11 | 2 | 0 | 12 |
| Week 16 Improved (n=66,9,1,67) | 8 | 1 | 0 | 12 |
| Week 24 Improved (n=66,9,1,67) | 8 | 1 | 0 | 12 |
| Week 40 Improved (n=66,9,1,67) | 8 | 2 | 0 | 9 |

Statistical analyses

| | |
|--|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 2: Data were compared statistically across all 3 categories (worsened, no change and improved). P-value was based on Cochran-Mantel-Haenszel (CMH) test for row mean scores differ, using change from baseline category as the score in the analysis, and stratified by the combinations of the 2 stratification factors (tumor aggressiveness and concomitant anticancer treatment). | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 133 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.709 |
| Method | Cochran-Mantel-Haenszel |

| | |
|--|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 4: Data were compared statistically across all 3 categories (worsened, no change and improved). P-value was based on Cochran-Mantel-Haenszel (CMH) test for row mean scores differ, using change from baseline category as the score in the analysis, and stratified by the combinations of the 2 stratification factors (tumor aggressiveness and concomitant anticancer treatment). | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 133 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.6103 |
| Method | Cochran-Mantel-Haenszel |

| | |
|--|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 8: Data were compared statistically across all 3 categories (worsened, no change and improved). P-value was based on Cochran-Mantel-Haenszel (CMH) test for row mean scores differ, using change from baseline category as the score in the analysis, and stratified by the combinations of the 2 stratification factors (tumor aggressiveness and concomitant anticancer treatment). | |
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 133 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.5272 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
| Statistical analysis description: | |
| Week 12: Data were compared statistically across all 3 categories (worsened, no change and improved). P-value was based on Cochran-Mantel-Haenszel (CMH) test for row mean scores differ, using change from baseline category as the score in the analysis, and stratified by the combinations of the 2 stratification factors (tumor aggressiveness and concomitant anticancer treatment). | |

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 133 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.5272 |
| Method | Cochran-Mantel-Haenszel |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

Week 16: Data were compared statistically across all 3 categories (worsened, no change and improved). P-value was based on Cochran-Mantel-Haenszel (CMH) test for row mean scores differ, using change from baseline category as the score in the analysis, and stratified by the combinations of the 2 stratification factors (tumor aggressiveness and concomitant anticancer treatment).

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 133 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.8723 |
| Method | Cochran-Mantel-Haenszel |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

Week 24: Data were compared statistically across all 3 categories (worsened, no change and improved). P-value was based on Cochran-Mantel-Haenszel (CMH) test for row mean scores differ, using change from baseline category as the score in the analysis, and stratified by the combinations of the 2 stratification factors (tumor aggressiveness and concomitant anticancer treatment).

| | |
|---|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
| Number of subjects included in analysis | 133 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.9982 |
| Method | Cochran-Mantel-Haenszel |

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | Placebo vs Tanezumab 20mg |
|-----------------------------------|---------------------------|

Statistical analysis description:

Week 40: Data were compared statistically across all 3 categories (worsened, no change and improved). P-value was based on Cochran-Mantel-Haenszel (CMH) test for row mean scores differ, using change from baseline category as the score in the analysis, and stratified by the combinations of the 2 stratification factors (tumor aggressiveness and concomitant anticancer treatment).

| | |
|-------------------|---------------------------|
| Comparison groups | Placebo v Tanezumab 20 mg |
|-------------------|---------------------------|

| | |
|---|-------------------------|
| Number of subjects included in analysis | 133 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.8823 |
| Method | Cochran-Mantel-Haenszel |

Secondary: Change From Screening in Mean Total Symptom Impact Score as Per Survey of Autonomic Symptoms (SAS) at Week 24, 48, Early Termination Visit 1 and 3

| | |
|-----------------|--|
| End point title | Change From Screening in Mean Total Symptom Impact Score as Per Survey of Autonomic Symptoms (SAS) at Week 24, 48, Early Termination Visit 1 and 3 |
|-----------------|--|

End point description:

The 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 on 5 point scale (1 [least sever impact] to 5 [most severe impact]); higher scores = more severe impact of symptoms. The total impact score was the sum of all symptom rating scores, with 0 assigned where the subject did not have the particular symptom. The range for males =12 (no impact) to 60 (extreme impact); females =11 (no impact) to 55 (extreme impact); higher scores = more severe impact of symptoms on subjects well-being. Subjects discontinuing from study treatment before Week 24 had early termination visits. mITT analysis set analysed. 99999= no subjects were analysed. N:subjects evaluable for endpoint. n:subjects evaluable at specified time points.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Screening, Week 24, 48, Early Termination Visit 1 (at 8 weeks after last dose of tanezumab or placebo) and Early Termination Visit 3 (at 24 weeks after last dose of tanezumab or placebo)

| End point values | Placebo | Tanezumab 10 mg | Tanezumab 10/20 mg | Tanezumab 20 mg |
|--|-----------------|-----------------|--------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 9 | 1 | 70 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Screening (n=73,9,1,70) | 1.11 (± 1.42) | 1.89 (± 1.96) | 1.00 (± 99999) | 1.00 (± 1.26) |
| Change at Week 24 (n=36,5,0,37) | 0.00 (± 1.57) | -0.20 (± 1.92) | 99999 (± 99999) | 0.46 (± 1.27) |
| Change at Week 48 (n=29,5,0,24) | -0.03 (± 0.91) | -0.20 (± 2.68) | 99999 (± 99999) | 0.42 (± 1.44) |
| Change at Early Termination Visit 1 (n=6,3,0,11) | 1.33 (± 2.34) | 1.67 (± 6.03) | 99999 (± 99999) | 0.36 (± 1.86) |
| Change at Early Termination Visit 3 (n=1,0,0,2) | 2.00 (± 99999) | 99999 (± 99999) | 99999 (± 99999) | 2.50 (± 2.12) |

Statistical analyses

No statistical analyses for this end point

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

| | |
|---|--|
| End point title | Number of Subjects With Anti-Drug Antibodies (ADA) and Neutralising Anti-Drug Antibodies (NAb) |
| End point description: | |
| Human serum ADA samples were analysed for the presence or absence of anti-tanezumab antibodies by using a semi quantitative enzyme linked immunosorbent assay (ELISA). Number of subjects with presence of anti-tanezumab antibodies and neutralising anti-drug antibodies are reported. The safety analysis set included all subjects treated with tanezumab or placebo SC, including subjects who received tanezumab 10 mg prior to protocol amendment 3. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Day 1, before dosing) up to Week 48 | |

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

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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

Adverse event reporting additional description:

Same event may appear as AE and SAE, what is presented are distinct events. Event may be categorised as serious in 1 subject and as non-serious in another subject or 1 subject may have experienced both serious and non-serious event during study. Safety analysis set was evaluated.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

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

| | |
|-----------------------|-----------------|
| Reporting group title | Tanezumab 20 mg |
|-----------------------|-----------------|

Reporting group description:

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

| | |
|-----------------------|--------------------|
| Reporting group title | Tanezumab 10/20 mg |
|-----------------------|--------------------|

Reporting group description:

Subjects in this treatment group had received tanezumab 10 mg SC once every 8 weeks before protocol amendment 3 and after the amendment they continued remaining treatment with tanezumab 20 mg SC once every 8 weeks.

| | |
|-----------------------|-----------------|
| Reporting group title | Tanezumab 10 mg |
|-----------------------|-----------------|

Reporting group description:

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

| Serious adverse events | Placebo | Tanezumab 20 mg | Tanezumab 10/20 mg |
|---|------------------|------------------|--------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 28 / 73 (38.36%) | 39 / 72 (54.17%) | 1 / 1 (100.00%) |
| number of deaths (all causes) | 3 | 3 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Bladder neoplasm | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast cancer | | | |

| | | | |
|---|----------------|----------------|---------------|
| subjects affected / exposed | 5 / 73 (6.85%) | 3 / 72 (4.17%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast cancer metastatic | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cancer pain | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 2 / 72 (2.78%) | 0 / 1 (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 |
| Colorectal cancer | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric cancer | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 1 / 72 (1.39%) | 0 / 1 (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 |
| Laryngeal cancer | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | 4 / 72 (5.56%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Metastases to bone | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 73 (1.37%) | 3 / 72 (4.17%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to central nervous system | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| Metastases to meninges | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neoplasm prostate | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatic carcinoma | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatic neoplasm | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostate cancer | | | |
| subjects affected / exposed | 7 / 73 (9.59%) | 7 / 72 (9.72%) | 1 / 1 (100.00%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 7 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |

| | | | |
|--|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Bronchitis chronic | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (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 |
| Pleurisy | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 2 / 72 (2.78%) | 0 / 1 (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 |

| | | | |
|---|----------------|----------------|---------------|
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Foot fracture | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal compression fracture | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebrovascular insufficiency | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Paraparesis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 2 / 72 (2.78%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Radiculopathy | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 73 (4.11%) | 3 / 72 (4.17%) | 1 / 1 (100.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|---------------|
| Flatulence | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Jaundice | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteonecrosis of jaw | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pathological fracture | | | |

| | | | |
|---|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 3 / 73 (4.11%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Hypophagia | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|-----------------|--|--|
| Serious adverse events | Tanezumab 10 mg | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Bladder neoplasm | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Breast cancer | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Breast cancer metastatic | | | |

| | | | | |
|---|---------------|--|--|--|
| subjects affected / exposed | 0 / 9 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cancer pain | | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colon cancer | | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colorectal cancer | | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastric cancer | | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Laryngeal cancer | | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lung neoplasm malignant | | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metastases to bone | | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metastases to central nervous system | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metastases to meninges | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neoplasm prostate | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatic carcinoma | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatic neoplasm | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Prostate cancer | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peripheral ischaemia | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Bronchitis chronic | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pleurisy | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 9 (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 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal compression fracture | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Cerebrovascular insufficiency | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Paraparesis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Radiculopathy | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 9 (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 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Flatulence | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Jaundice | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 9 (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 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Osteonecrosis of jaw | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pathological fracture | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|--|---------------------------------|--|--|
| Infections and infestations Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 9 (0.00%) 0 / 0 0 / 0 | | |
| Sepsis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 9 (0.00%) 0 / 0 0 / 0 | | |
| Metabolism and nutrition disorders Hypophagia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 9 (0.00%) 0 / 0 0 / 0 | | |

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

| Non-serious adverse events | Placebo | Tanezumab 20 mg | Tanezumab 10/20 mg |
|---|------------------|------------------|--------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 43 / 73 (58.90%) | 49 / 72 (68.06%) | 1 / 1 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast cancer | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | 4 / 72 (5.56%) | 0 / 1 (0.00%) |
| occurrences (all) | 2 | 5 | 0 |
| Cancer pain | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 2 / 72 (2.78%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metastases to bone | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Neoplasm | | | |

| | | | |
|---|---------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 73 (0.00%) 0 | 0 / 72 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Prostate cancer subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 2 | 3 / 72 (4.17%) 3 | 0 / 1 (0.00%) 0 |
| Vascular disorders | | | |
| Hypertension subjects affected / exposed occurrences (all) | 1 / 73 (1.37%) 1 | 2 / 72 (2.78%) 2 | 0 / 1 (0.00%) 0 |
| Lymphoedema subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 2 | 0 / 72 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Orthostatic hypotension subjects affected / exposed occurrences (all) | 1 / 73 (1.37%) 1 | 1 / 72 (1.39%) 1 | 0 / 1 (0.00%) 0 |
| Pallor subjects affected / exposed occurrences (all) | 0 / 73 (0.00%) 0 | 2 / 72 (2.78%) 2 | 0 / 1 (0.00%) 0 |
| General disorders and administration site conditions | | | |
| Asthenia subjects affected / exposed occurrences (all) | 4 / 73 (5.48%) 4 | 6 / 72 (8.33%) 9 | 1 / 1 (100.00%) 1 |
| Fatigue subjects affected / exposed occurrences (all) | 5 / 73 (6.85%) 7 | 6 / 72 (8.33%) 6 | 1 / 1 (100.00%) 1 |
| Influenza like illness subjects affected / exposed occurrences (all) | 1 / 73 (1.37%) 1 | 4 / 72 (5.56%) 5 | 0 / 1 (0.00%) 0 |
| Oedema peripheral subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 2 | 9 / 72 (12.50%) 9 | 0 / 1 (0.00%) 0 |
| Pain subjects affected / exposed occurrences (all) | 3 / 73 (4.11%) 4 | 6 / 72 (8.33%) 8 | 0 / 1 (0.00%) 0 |
| Peripheral swelling | | | |

| | | | |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 73 (1.37%) 1 | 2 / 72 (2.78%) 2 | 0 / 1 (0.00%) 0 |
| Pyrexia subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 2 | 2 / 72 (2.78%) 2 | 0 / 1 (0.00%) 0 |
| Immune system disorders Contrast media allergy subjects affected / exposed occurrences (all) | 0 / 73 (0.00%) 0 | 0 / 72 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 2 | 2 / 72 (2.78%) 2 | 0 / 1 (0.00%) 0 |
| Dyspnoea subjects affected / exposed occurrences (all) | 3 / 73 (4.11%) 3 | 3 / 72 (4.17%) 5 | 0 / 1 (0.00%) 0 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 2 | 0 / 72 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Pulmonary mass subjects affected / exposed occurrences (all) | 0 / 73 (0.00%) 0 | 0 / 72 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Wheezing subjects affected / exposed occurrences (all) | 0 / 73 (0.00%) 0 | 0 / 72 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 3 / 73 (4.11%) 3 | 0 / 72 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Depressed mood subjects affected / exposed occurrences (all) | 3 / 73 (4.11%) 5 | 2 / 72 (2.78%) 5 | 1 / 1 (100.00%) 1 |
| Depression subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 2 | 2 / 72 (2.78%) 2 | 0 / 1 (0.00%) 0 |
| Insomnia | | | |

| | | | |
|--|---------------------|---------------------|--------------------|
| subjects affected / exposed occurrences (all) | 1 / 73 (1.37%) 1 | 5 / 72 (6.94%) 5 | 0 / 1 (0.00%) 0 |
| Investigations | | | |
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 4 | 0 / 72 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Weight decreased subjects affected / exposed occurrences (all) | 3 / 73 (4.11%) 3 | 3 / 72 (4.17%) 3 | 0 / 1 (0.00%) 0 |
| Weight increased subjects affected / exposed occurrences (all) | 0 / 73 (0.00%) 0 | 0 / 72 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| White blood cell count decreased subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 6 | 0 / 72 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Fall subjects affected / exposed occurrences (all) | 3 / 73 (4.11%) 4 | 5 / 72 (6.94%) 7 | 0 / 1 (0.00%) 0 |
| Toxicity to various agents subjects affected / exposed occurrences (all) | 0 / 73 (0.00%) 0 | 0 / 72 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Nervous system disorders | | | |
| Dizziness subjects affected / exposed occurrences (all) | 3 / 73 (4.11%) 3 | 3 / 72 (4.17%) 4 | 0 / 1 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 2 | 5 / 72 (6.94%) 5 | 0 / 1 (0.00%) 0 |
| Neuralgia subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 4 | 2 / 72 (2.78%) 3 | 0 / 1 (0.00%) 0 |
| Paraesthesia subjects affected / exposed occurrences (all) | 0 / 73 (0.00%) 0 | 2 / 72 (2.78%) 6 | 0 / 1 (0.00%) 0 |
| Somnolence | | | |

| | | | |
|--|---------------------|---------------------|--------------------|
| subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 2 | 2 / 72 (2.78%) 2 | 0 / 1 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 9 / 73 (12.33%) | 9 / 72 (12.50%) | 1 / 1 (100.00%) |
| occurrences (all) | 9 | 10 | 2 |
| Leukopenia | | | |
| subjects affected / exposed | 3 / 73 (4.11%) | 2 / 72 (2.78%) | 0 / 1 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eye disorders | | | |
| Visual acuity reduced | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal hernia | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 3 / 73 (4.11%) | 6 / 72 (8.33%) | 1 / 1 (100.00%) |
| occurrences (all) | 3 | 6 | 1 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 6 / 72 (8.33%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 7 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 6 / 73 (8.22%) | 4 / 72 (5.56%) | 0 / 1 (0.00%) |
| occurrences (all) | 8 | 7 | 0 |
| Toothache | | | |

| | | | |
|--|-----------------------|------------------------|----------------------|
| subjects affected / exposed occurrences (all) | 4 / 73 (5.48%) 5 | 0 / 72 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Vomiting subjects affected / exposed occurrences (all) | 6 / 73 (8.22%) 7 | 4 / 72 (5.56%) 5 | 1 / 1 (100.00%) 1 |
| Skin and subcutaneous tissue disorders | | | |
| Decubitus ulcer subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 2 | 2 / 72 (2.78%) 2 | 0 / 1 (0.00%) 0 |
| Pruritus subjects affected / exposed occurrences (all) | 3 / 73 (4.11%) 3 | 2 / 72 (2.78%) 3 | 0 / 1 (0.00%) 0 |
| Rash subjects affected / exposed occurrences (all) | 4 / 73 (5.48%) 4 | 1 / 72 (1.39%) 1 | 0 / 1 (0.00%) 0 |
| Renal and urinary disorders | | | |
| Dysuria subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 2 | 0 / 72 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Urinary incontinence subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 2 | 0 / 72 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 7 / 73 (9.59%) 18 | 11 / 72 (15.28%) 16 | 0 / 1 (0.00%) 0 |
| Back pain subjects affected / exposed occurrences (all) | 9 / 73 (12.33%) 14 | 1 / 72 (1.39%) 2 | 0 / 1 (0.00%) 0 |
| Myalgia subjects affected / exposed occurrences (all) | 1 / 73 (1.37%) 1 | 0 / 72 (0.00%) 0 | 0 / 1 (0.00%) 0 |
| Osteoarthritis subjects affected / exposed occurrences (all) | 1 / 73 (1.37%) 1 | 2 / 72 (2.78%) 2 | 0 / 1 (0.00%) 0 |
| Pain in extremity | | | |

| | | | |
|------------------------------------|----------------|------------------|-----------------|
| subjects affected / exposed | 5 / 73 (6.85%) | 3 / 72 (4.17%) | 0 / 1 (0.00%) |
| occurrences (all) | 6 | 4 | 0 |
| Pathological fracture | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 3 / 72 (4.17%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Infections and infestations | | | |
| Bacterial infection | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 2 / 72 (2.78%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 2 / 72 (2.78%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 4 / 72 (5.56%) | 0 / 1 (0.00%) |
| occurrences (all) | 2 | 4 | 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 3 / 72 (4.17%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 1 / 72 (1.39%) | 1 / 1 (100.00%) |
| occurrences (all) | 1 | 1 | 1 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 4 / 73 (5.48%) | 10 / 72 (13.89%) | 1 / 1 (100.00%) |
| occurrences (all) | 5 | 10 | 2 |
| Dehydration | | | |

| | | | |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 73 (0.00%) | 2 / 72 (2.78%) | 1 / 1 (100.00%) |
| occurrences (all) | 0 | 2 | 1 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 3 / 73 (4.11%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 3 / 73 (4.11%) | 1 / 72 (1.39%) | 0 / 1 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | 0 / 72 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |

| | | | |
|---|-----------------|--|--|
| Non-serious adverse events | Tanezumab 10 mg | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 9 (88.89%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast cancer | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Metastases to bone | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Neoplasm | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vascular disorders | | | |

| | | | |
|--|----------------|--|--|
| Hypertension | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lymphoedema | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Pallor | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 5 | | |
| Influenza like illness | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Immune system disorders | | | |

| | | | |
|--|--|--|--|
| Contrast media allergy subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Pulmonary mass subjects affected / exposed occurrences (all) Wheezing subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 2 / 9 (22.22%) 2 0 / 9 (0.00%) 0 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1 | | |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Depressed mood subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 0 / 9 (0.00%) 0 0 / 9 (0.00%) 0 1 / 9 (11.11%) 1 | | |
| Investigations Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |

| | | | |
|--|---------------------|--|--|
| Weight decreased subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Weight increased subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| White blood cell count decreased subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Toxicity to various agents subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Headache subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Neuralgia subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Paraesthesia subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Somnolence subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |

| | | | |
|--|---------------------|--|--|
| Leukopenia subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Eye disorders Visual acuity reduced subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Gastrointestinal disorders Abdominal hernia subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Constipation subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 2 | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Dyspepsia subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Gastritis subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Nausea subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Toothache subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|---------------------|--|--|
| Decubitus ulcer subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Pruritus subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 2 | | |
| Rash subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Urinary incontinence subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 2 | | |
| Back pain subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Myalgia subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | | |
| Osteoarthritis subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Pathological fracture subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | | |
| Infections and infestations | | | |

| | | | |
|------------------------------------|----------------|--|--|
| Bacterial infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cystitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypokalaemia | | | |

| | | | |
|-----------------------------|---------------|--|--|
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | | |
| occurrences (all) | 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

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

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported