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GENERIC DRUG NAME and/or COMPOUND NUMBER: Tanezumab/PF-04383119

THERAPEUTIC AREA AND FDA APPROVED INDICATIONS: Not Applicable

NATIONAL CLINICAL TRIAL NO.: NCT00826514

PROTOCOL NO.: A4091019

PROTOCOL TITLE: A Phase 2, 16 Week, Multicenter, Randomized, Double-Blind Placebo-Controlled, Parallel Group Proof-of-Concept Study Evaluating the Efficacy and Safety of Tanezumab for the Treatment of Pain Associated with Chronic Abacterial Prostatitis

Study Center(s): This study was conducted at 7 study centers in Canada, 4 centers in France, 1 center in Sweden, 2 centers in Switzerland, and 16 centers in the United States.

Study Initiation Date and Primary Completion or Completion Dates: 25 March 2009 to 17 March 2010

Phase of Development: Phase 2

Study Objective(s): The primary objective was to evaluate the efficacy, safety and tolerability of a single 5-minute intravenous (IV) injection of tanezumab in the treatment of pain associated with chronic prostatitis (CP).
The secondary objective was to evaluate the efficacy of a single dose of tanezumab in the treatment of other symptoms (eg, urinary urgency and frequency) associated with CP.

METHODS

Study Design: This was a randomized, double-blind, placebo-controlled, parallel group, proof-of-concept study. Overall, 48 subjects suffering from CP (24 per group) were planned to complete the study. Subjects entering the treatment phase were randomized to receive a single dose of tanezumab 20 mg IV, or placebo IV in a 1:1 ratio.

The study consisted of a 2-week assessment period followed by a 16-week double-blind randomized treatment period. Following screening assessments, eligible subjects entered a 2-week diary assessment period. The subject's daily pain numeric ratings scale (NRS) was collected via interactive voice response system (IVRS) commencing from the evening of the first day of the screening assessment period, and was used to assess inclusion into the study and to determine stratification at randomization. In addition, subjects completed a 3-day urinary symptom diary within a 7-day period prior to the randomization visit. At

Assessment 2, subjects were stratified and randomized, and subsequently received a single dose of tanezumab or placebo. The double-blind treatment period included 5 clinic visits (Assessments 2, 3, 5, 7 and 8) and 2 self-reported assessments (Assessments 4 and 6), which were conducted on an outsubject basis.

During both, assessment and treatment period subjects were provided with rescue medication in the form of approved acetaminophen/paracetamol 500 mg tablets or capsules.

Number of Subjects (Planned and Analyzed): The planned sample size was 74 subjects recruited in order to obtain 48 evaluable subjects (24 per treatment arm), assuming a 35% drop-out rate. Sixty-two (62) subjects were enrolled, and all of them were dosed with either placebo (32 subjects) or tanezumab (30 subjects).

Diagnosis and Main Criteria for Inclusion: Male subjects ≥18 years of age weighing ≤160 kg or with a body mass index (BMI) of ≤39 kg/m^2. Subjects had to have moderate to severe abacterial CP or chronic pelvic pain syndrome (CPPS) at screening as defined by a chronic prostatitis symptom index (CPSI) total score ≥15 and a negative 4-glass test within 2 years of screening. At the randomization visit, subjects had to have completed ≥4 diary days during the 7 days before randomization, with a mean average pain intensity score of ≥4 (0-10 on the NRS).

Study Treatment: Subjects were stratified based on their average daily pain NRS score from the initial pain assessment period 7 days prior to randomization, and then randomized to either treatment with tanezumab or treatment with placebo in a 1:1 ratio. Subjects were stratified according to a computer-generated pseudorandom code using the method of random permuted blocks. The randomization number assigned to the subject was provided by the system. Subjects received a single 5-minute IV injection of tanezumab 20 mg, or a single 5-minute IV injection of placebo. Tanezumab or placebo was administered by a slow 5-minute IV injection without using an infusion pump, followed by an IV flush of 5 mL sodium chloride injection.

Efficacy Evaluations: The primary efficacy endpoint was the change from baseline to Week 6 in 24-hour average pain score as measured by an 11-point NRS.

Secondary Endpoints: Secondary endpoints were worst daily pain score and average daily pain score at time points other than Week 6 (as measured by an 11-point NRS), National Institute of Health (NIH) CPSI score (overall and pain, urinary symptoms and quality of life sub-scores), sleep disturbance, ejaculatory pain, micturition diary variables (micturition frequency, nocturnal frequency, mean voided volume, urgency episode frequency [UEF] per 24 hours, and mean pain severity per urinary event), global response assessment (GRA), patient reported treatment impact (PRTI), responder rates (with regard to average daily pain score and to GRA response, respectively), and rescue medication use.

Pharmacokinetic, Pharmacodynamic, and/or Other Evaluations: Pharmacokinetic (PK) blood samples were collected at randomization (at predose, postdose [end infusion] and 2 hours postdose), Week 2, Week 6, Week 10, and Week 16, or at early termination. Blood samples for the assessment of anti-tanezumab antibodies (ADA) were collected at

randomization (predose), Week 2, Week 6, and Week 16, or at early termination. Blood and urine samples for biomarkers (nerve growth factor [NGF]) were collected at screening, randomization (predose), Week 2, Week 6, Week 10 and Week 16, or at early termination. All samples were stored at approximately -70^{o}C until assayed. Plasma tanezumab and ADA concentrations were determined using a validated, sensitive and specific enzyme-linked immunosorbent assay (ELISA). NGF serum concentrations were determined using high performace liquid chromatography – tandem mass spectrometry (HPLC-MS/MS).

Safety Evaluations: Adverse events (AEs) were documented throughout the study. Neurological examinations were to be performed at screening, randomization (predose), and at Weeks 2, 6, 10, and 16 (or at early termination). The investigator was to complete the Neuropathy Impairment Score (NIS) at these time points based on the neurological examination. Investigators attended a training session for neurological examinations to apply consistency across sites. A neurological evaluation was to be performed by a consulting neurologist if AEs suggested new or worsening peripheral neuropathy or any AE of abnormal peripheral sensation (eg, allodynia, dysaesthesia). In addition, neurological consultations were to occur if subjects had pain in the extremities (eg, fingers, hands, feet, soles of feet) suggestive of neuropathic pain, or if a new or worsened clinically significant abnormality on the neurological examination were reported during the study. A neurological evaluation was to be done as soon as the above signs and symptoms were known, preferably within 7 days of becoming aware of such problems if possible. In addition, vital signs, weight measurement, physical examinations, concomitant medications, postvoid residual (PVR) volume, electrocardiograms (ECGs), hospital anxiety and depression scale (HADS), laboratory safety tests, pregnancy testing, 4-glass culture, urine Chlamydia testing and urinalysis were collected for each subject during the study.

Statistical Methods: The full analysis set (FAS) was defined as all randomized subjects, who received at least 1 dose of study treatment (either tanezumab or placebo), and who completed at least 4 diary days during the 7 days prior to randomization. The restricted FAS (rFAS) was defined as all FAS subjects, for whom baseline and postrandomization primary efficacy data for 4 or more days within the predefined assessment windows, or for 2 or more consecutive days for diary endpoints derived from the 3-day diary, were available. The per protocol (PP) analysis set was defined as all FAS subjects, who completed the study up to Assessment 5, had not violated any inclusion/exclusion criteria affecting efficacy prior to randomization, and who had no major deviations from the protocol affecting efficacy in the postrandomization period.

The primary analysis was based on the rFAS for the following reasons: this was a proof-of-concept study, the primary endpoint was diary-based and may have been incomplete for some subjects, and ensured that subjects included in the primary analysis had adequate posttreatment diary data. The secondary analyses were based on the unrestricted FAS and the PP analysis set.

The primary efficacy endpoint was the change from baseline to Week 6 in 24-hour average pain score as measured by an 11-point NRS. This was calculated by determining the average of the pain scores recorded in the 7 days prior to each assessment point. In this exploratory proof-of-concept study, no formal statistical hypothesis was tested. The differences between

treatment means, the standard errors associated with the differences and 90% confidence intervals (CIs) for the differences were presented.

The primary endpoint was analyzed using an analysis of covariance (ANCOVA) model, with terms for baseline value, treatment, age and baseline severity of pain score.

The secondary endpoints worst daily pain score and average daily pain score at time points other than Week 6, NIH CPSI scores, sleep disturbance, ejaculatory pain, micturition diary variables, GRA, PRTI, and responder rates were considered continuous for this study, and were analyzed from baseline to each time point using ANCOVA, with terms for baseline value, treatment, age and baseline severity of pain score. Rescue medication use was descriptively presented using Kaplan-Meier curves and estimates for the median time to event and corresponding 90% CIs.

Plasma tanezumab concentrations, ADA serum concentration, and NGF levels were listed and summarized by assessment point and treatment.

Safety data was presented for the safety analysis set (SAS). The SAS was defined as all subjects who received at least 1 dose of study treatment. Standard reporting tables were used to summarize and list safety results. Additional nonstandard safety assessments included neurological examinations and neurological consultations. AEs were coded using the Medical Dictionary for Regulatory Activities (MedDRA) Version 13.0. No formal hypothesis testing of safety data was performed.

RESULTS

Subject Disposition and Demography: One hundred and sixty-four (164) subjects were screened for this study. In total, 62 subjects were assigned to the treatment. All of them received treatment: There were 30 subjects in the tanezumab group and 32 subjects in the placebo treatment group. Twenty-seven (27) subjects (90.0% of randomized subjects) in the tanezumab treatment group, and 27 subjects (84.4%) in the placebo treatment group completed the study (Week 16).

In the tanezumab and placebo treatment groups, 3 subjects (10.0%) and 5 subjects (15.6%), respectively, discontinued the study. One subject in the placebo group discontinued because of lack of efficacy. One subject in each treatment group withdrew from the study due to an AE. The AEs were assessed as unrelated to study treatment for both subjects. A total of 5 subjects, 2 (6.7%) in the tanezumab and 3 (9.4%) in the placebo group voluntarily withdrew from the study. When reasons were given for withdrawal of consent they were mostly personal in nature, generally having to do with lack of time for study visits.

Subject disposition is summarized in Table 1.

Table 1. Subject Disposition

Number (%) of subjects	Tanezumab	Placebo
Screened: 164		
Assigned to study treatment	30	32
Treated	30	32
Completed Week 6 visit	29 (96.7)	30 (93.8)
Completed Week 16 visit	27 (90.0)	27 (84.4)
Discontinued [a]	3 (10.0)	5 (15.6)
Related to study drug	0	1 (3.1)
Lack of efficacy	0	1 (3.1)
Not related to study drug	3 (10.0)	4 (12.5)
Adverse event	1 (3.3)	1 (3.1)
Subject no longer willing to participate	2 (6.7)	3 (9.4)

Discontinuations occurring outside the lag period were attributed to the last study treatment received.
[a] Denominator used for calculating percentages is the number of patients treated.

All subjects who were randomized and received treatment were included in the FAS and the safety analyses (Table 2). The rFAS used for the analysis of Week 6 changes for endpoints based on the daily symptom diary included 27 subjects (90.0%) in the tanezumab and 28 subjects (87.5%) in the placebo group. Slightly fewer subjects were available in the rFAS for the Week 6 analysis of urinary endpoints. The PP analysis set included 25 subjects (83.3%) in the tanezumab and 25 subjects (78.1%) in the placebo groups, respectively.

Table 2. Data Sets Analyzed

Number (%) of subjects	Tanezumab N = 30	Placebo N = 32
Assigned to study treatment	30	32
Treated	30	32
Analyzed for efficacy		
FAS	30 (100.0)	32 (100.0)
rFAS Week 6 (daily symptom diary)	27 (90.0)	28 (87.5)
rFAS Week 6 (urinary event diary)	23 (76.7)	26 (81.3)
PP analysis set	25 (83.3)	25 (78.1)
Analyzed for safety		
AEs	30 (100.0)	32 (100.0)
Laboratory data	30 (100.0)	32 (100.0)
Safety analysis set	30 (100.0)	32 (100.0)

AE = adverse event, FAS = full analysis set, N = number of subjects in respective treatment group, PP = per protocol, rFAS = restricted full analysis set.

Baseline subject characteristics were generally similar across treatment groups. All subjects included in the study were male (Table 3). The mean age was slightly higher in the tanezumab group (50.5 years) than in the placebo group (43.2 years). The mean weight was comparable for the tanezumab (88.7 kg) and the placebo (86.6 kg) groups. Across the treatment groups, subjects were mostly White. The mean duration (range) of prostatitis symptoms at randomization was 6.5 years (0.3 to 30.1 years) in the tanezumab treatment group and 5.6 years (0.4 to 23.9 years) in the placebo treatment group.

Table 3. Subject Demographics

	Tanezumab N = 30	Placebo N = 32
Gender, n (%)		
Male	30 (100.0)	32 (100.0)
Age [years]		
Mean (SD)	50.5 (11.9)	43.2 (13.5)
Range	28-72	21-72
Race, n (%)		
White	29 (96.7)	26 (81.3)
Black	1 (3.3)	5 (15.6)
Other	0	1 (3.1)
Weight [kg]		
Mean (SD)	88.7 (14.2)	86.6 (12.4)
Range	60.3-131.5	68.7-130.0
Height [cm]		
Mean (SD)	177.4 (6.6)	175.9 (8.7)
Range	165.0-189.0	152.0-193.0
Body Mass Index [kg/m^2]		
Mean (SD)	28.2 (4.2)	28.0 (3.3)
Range	21.9-41.5	20.2-34.9
Duration of prostatitis since first diagnosis [years][a]	30 (100.0)	32 (100.0)
Mean	3.6	4.1
Range	0.1-20.7	0.0-20.0
Unspecified [n]	1	0
Duration of prostatitis since symptom onset [years][a]		
Mean	6.5	5.6
Range	0.3-30.1	0.4-23.9
Prostatitis classification, n (%)		
IIIa	7 (23.33)	5 (15.63)
IIIb	22 (73.33)	23 (71.88)
Missing	1 (3.33)	4 (12.50)

[a] Duration from first diagnosis to Day 1 of study.
N = number of subjects in respective treatment group, n= number of subjects with respective characteristic, SD = standard deviation.

All subjects assigned to treatment (30 in the tanezumab and 32 in the placebo groups) received a single dose of either 20 mg tanezumab or placebo at the randomization visit.

Efficacy Results: Primary Evaluation: The clinically significant level of change in average pain intensity over placebo is not known for CP, although for other chronic pain conditions such as lower back pain and interstitial cystitis it is thought to lie at 0.7 or greater. There was an improvement at Week 6 compared to baseline in the average pain intensity per 24 hours for both treatment groups according to the rFAS analysis (Table 4). The decrease in average pain intensity from baseline to Week 6 was larger with tanezumab treatment relative to placebo treatment, but this difference (-0.47) was not statistically proven using 90% CIs.

Table 4. Change from Baseline to Week 6 in Average Pain Intensity per 24 Hours (rFAS)

			N	Tanezumab	N	Placebo
Baseline mean (SD)			30	5.5 (1.10)	31	5.6 (1.14)
			Difference versus placebo[a]			
	N	LS Mean (SE)	LS Mean Diff. (SE of Diff.)		90% CI	
Tanezumab	27	-1.46 (0.285)	-0.47 (0.392)		-1.150, 0.209	
Placebo	28	-0.99 (0.279)				

[a]ANCOVA model with baseline value of the endpoint, age, and treatment as covariates.
ANCOVA = analysis of covariance, CI = confidence interval, Diff. = difference, LS = least squares, N = number of subjects with data available, rFAS = restricted Full Analysis Set, SE = standard error, SD = standard deviation.

Secondary Evaluations: The results of the analyses of secondary endpoints generally followed those seen for the primary endpoint. A summary of the results for selected secondary endpoints is provided in Table 5. The tanezumab treatment group showed a trend for a larger improvement from baseline to Week 6 in worst daily pain score compared to placebo. The reduction in the CPSI pain domain score, quality of life score and total CPSI score was more pronounced in the tanezumab group than in the placebo group, but was less pronounced in the tanezumab than in the placebo group for the urinary symptom score. None of the treatment differences were statistically proven based on 90% CIs. No relevant difference between the treatment groups was shown for ejaculatory pain from baseline to Week 6. While the reduction in nocturnal frequency per night from baseline to Week 6 was slightly larger in the tanezumab than in the placebo group, the opposite was seen for the micturition frequency per 24 hours, although the CIs were fairly evenly spread across zero. A difference in favor of placebo treatment was shown for the change in mean voided volume per micturition from baseline to Week 6. A more pronounced decrease from baseline to Week 6 with tanezumab compared to placebo treatment was shown for the mean urinary event pain score and the UEF.

Table 5. Change from Baseline to Week 6 in Selected Secondary Efficacy Endpoints (rFAS)

			Difference versus placebo[a]	
	N	LS Mean (SE)	LS Mean Diff. (SE of Diff.)	90% CI
Worst Daily Pain NRS Score				
Tanezumab	27	-1.32 (0.444)	-0.36 (0.469)	-1.188, 0.463
Placebo	28	-0.96 (0.467)		
NIH CPSI - pain domain score				
Tanezumab	25	-2.77 (0.901)	-1.06 (0.931)	-2.701, 0.591
Placebo	26	-1.71 (1.013)		
NIH CPSI - urinary symptom score				
Tanezumab	25	-0.44 (0.653)	0.38 (0.670)	-0.789, 1.541
Placebo	26	-0.82 (0.696)		
NIH CPSI - quality of life score				
Tanezumab	25	-1.07 (0.671)	-0.58 (0.697)	-1.785, 0.631
Placebo	26	-0.50 (0.722)		
NIH CPSI - total score				
Tanezumab	25	-4.26 (1.831)	-1.42 (1.901)	-4.754, 1.905
Placebo	26	-2.83 (1.975)		
Ejaculatory pain				
Tanezumab	13	-1.21 (0.601)	0.02 (0.765)	-1.791, 1.822
Placebo	10	-1.23 (0.883)		
Micturition frequency per 24 hours				
Tanezumab	23	-0.35 (0.664)	0.18 (0.649)	-0.990, 1.348
Placebo	26	-0.53 (0.718)		
Nocturnal frequency per night				
Tanezumab	23	-1.16 (0.915)	-0.19 (0.930)	-1.829, 1.452
Placebo	23	-0.97 (1.018)		
Mean voided volume per micturition (mL)				
Tanezumab	23	-22.47 (17.168)	-33.56 (17.026)	-64.144, -2.968
Placebo	26	11.09 (18.942)		
Mean urinary event pain score				
Tanezumab	23	-1.07 (0.505)	-0.47 (0.489)	-1.364, 0.415
Placebo	26	-0.60 (0.541)		
Urinary urgency episodes per 24 hours				
Tanezumab	23	-1.40 (1.012)	-1.37 (0.990)	-3.146, 0.401
Placebo	26	-0.03 (1.095)		

[a]ANCOVA model with baseline value of the endpoint, age, baseline pain stratification group, and treatment as covariates.
ANCOVA = analysis of covariance, CI = confidence interval, Diff. = difference, LS = least squares, N = number of subjects with data available, NIH CPSI = National Institute of Health Chronic Prostatitis Symptom Index, NRS = numeric ratings scale, rFAS = restricted Full Analysis Set, SE = standard error, SD = standard deviation.

No relevant difference between the treatment groups was shown for the reduction in sleep disturbance score (LS Mean of difference: -0.04, 90% CI: -0.417 to 0.334) from baseline to Week 6.

A higher percentage of subjects in the tanezumab treatment group achieved a ≥30% reduction in average pain intensity per 24 hours (40.7%) compared to placebo treatment

(32.1%) at Week 6. The treatment groups were comparable for the percentage of subjects achieving a ≥50% reduction in average pain intensity at Week 6 (tanezumab: 18.5%, placebo: 17.9%). However, a notably higher percentage of subjects in the tanezumab group compared to the placebo group (18.5% and 3.6%, respectively) were responders based on the ≥50% reduction in worst pain score definition.

At Week 6, subjects in the tanezumab treatment group most frequently rated their CP symptoms as slightly improved (10 subjects, 40.0%), while subjects in the placebo group most frequently rated their CP symptoms as unchanged (11 subjects, 42.3%). According to the patient reported treatment impact questionnaire, subjects in both treatment groups most frequently were neither satisfied nor dissatisfied with their treatment (40.0% and 54.2%, respectively) at Week 6.

A slightly higher proportion of placebo-treated subjects than tanezumab-treated subjects used rescue medication during the first 8 days after treatment, indicating that rescue medication use was slightly delayed by tanezumab treatment.

Pharmacokinetic, Pharmacodynamic, and/or Other Results: In general, mean tanezumab concentrations appeared to increase 5 minutes to 2 hours postdose and to slowly decline afterwards. Following study medication infusion, total NGF plasma concentrations were elevated in the tanezumab treatment group compared to the placebo group. No ADAs were detected in any subject enrolled in this study.

Population PK/pharmacodynamic (PD) modeling results are reported separately.

Safety Results: The overall number of subjects with AEs was slightly higher in the tanezumab treatment group (24 of 30 subjects) than in the placebo treatment group (21 of 32 subjects). The overall number of AEs was also higher in the tanezumab than in the placebo treatment group. There were no deaths among subjects who participated in this study. Only 1 subject in the tanezumab treatment group experienced an SAE: 'device breakage' (the ceramic head of his hip prosthesis broke) at Day 52. The subject subsequently had a hip operation and discontinued the study. The SAE was not considered related to the study drug. Only 1 subject in each treatment group discontinued the study due to an AE. In the tanezumab group, device breakage (see above) led to study withdrawal of 1 subject. In the placebo group, 1 subject discontinued the study due to worsening of back pain. The intensity of the back pain was documented as severe. None of the 2 AEs was considered related to the study drug. No subject in the tanezumab or placebo treatment groups had a dose reduction or discontinued study drug temporarily due to an AE.

The incidence of the most frequently reported AEs (AEs reported by at least 2 subjects in either treatment group) is shown in Table 6. Among the most frequently reported AEs, paraesthesia, arthralgia, headache, pain in extremity, and allodynia were reported by at least 4 more subjects in the tanezumab treatment group than in the placebo treatment group.

Table 6. Most Common Treatment-Emergent AEs (≥2 Subjects in Any Treatment Group; All Causalities; SAS)

Number of subjects (%)[a]	Tanezumab N	Placebo N
Subjects evaluable for AEs	30	32
Subjects with AEs	24	21
Paraesthesia	8	2
Arthralgia	7	0
Headache	6	2
Pain in extremity	5	1
Allodynia	4	0
Insomnia	3	1
Diarrhoea	2	1
Limb discomfort	2	0
Muscle spasm	2	0
Myalgia	2	1
Dizziness	2	3
Hyperaesthesia	2	0
Somnolence	2	1
Rash	2	2
Flushing	2	0
Nausea	1	2
Back pain	1	2
Fatigue	0	2

[a] In at least 2 subjects in any treatment group at the preferred term level.
MedDRA (version 13.0) coding dictionary applied.
Subjects were counted only once per treatment for each row.
AE = adverse event, MedDRA = Medical Dictionary for Regulatory Activities, N = number of subjects, SAS = safety analysis set

AEs of abnormal peripheral sensation were reported more frequently in the tanezumab treatment group (12 of 30 subjects) than in the placebo treatment group (3 of 32 subjects). Paraesthesia, allodynia, and hyperaesthesia were the most frequent AEs of abnormal peripheral sensation documented in the tanezumab group. Paraesthesia occurred in 8 subjects in the tanezumab group, compared to 2 subjects in the placebo group. Allodynia and hyperaesthesia occurred in tanezumab-treated subjects only. Paraesthesia (oral), burning sensation, and formication were the only AEs of abnormal peripheral sensation reported in the placebo treatment group. The majority of AEs of abnormal peripheral sensation were assessed as treatment related by the investigator.

The incidence of selected AEs (arthralgia, myalgia, pain in extremity and peripheral oedema) was generally higher in the tanezumab treatment group than in the placebo treatment group. The majority of subjects with arthralgia, myalgia, pain in extremity, and peripheral oedema in the tanezumab treatment group also reported AEs of abnormal peripheral sensation.

A new, clinically significant abnormality at any postbaseline neurological examination was detected in 3 subjects in the tanezumab group and 1 subject in the placebo treatment group.

Clinically insignificant abnormalities were detected in 1 subject in the tanezumab and 2 subjects in the placebo treatment groups.

A neurological consultation was to be performed by a neurologist if a subject had a new or worsening peripheral neuropathy or any AE of abnormal peripheral sensation, or if the subject had a new or worsened clinically significant abnormality from the neurological examination. In total, 14 subjects, 12 in the tanezumab group and 2 in the placebo group, were referred for neurological consultation. Ten (10) tanezumab-treated subjects completed the consultation. For all of the 10 subjects undergoing neurological consultation at least 1 AE of abnormal peripheral sensation had been documented and for 3 subjects AEs of pain in extremity had been documented in addition. No subject in the placebo treatment group underwent a neurological consultation. New or worsened peripheral neuropathy was diagnosed during the consultation in 5 subjects (16.7%) in the tanezumab treatment group. Symptoms or signs suggestive of a preexisting neuropathy were identified at consultation in 1 subject in the tanezumab group (3.3%). For 4 subjects (13.3%), no neurological symptoms or signs were confirmed during the neurological consultation.

Generally, there were no notable median changes from baseline to last observation for any hematology, clinical chemistry, or urinalysis test values. Of subjects with normal baseline values, 4 subjects in the placebo treatment group had an elevated partial thromboplastin time (PTT) compared to no subject in the tanezumab group. All other abnormalities in subjects were reported in 1 or 2 subjects per treatment group only, without notable differences between the treatment groups. Mean changes in vital signs from baseline were small, and no trends were observed over time. A clinically significant change in ECG parameters from baseline was documented for 1 subject per treatment group only. A change in physical examination findings from screening was documented for 1 subject in the placebo treatment group. No relevant changes in postvoid residual volume were shown.

CONCLUSION(S):

- The efficacy results demonstrated a trend for a tanezumab treatment effect in reducing average daily pain score and UEF associated with CP. Some of the other indicators showed modest improvements for the tanezumab group compared to placebo.

- Overall, tanezumab was safe and well tolerated in this study with an AE profile similar to other tanezumab studies.

- Among the most commonly recorded AEs, paraesthesia, arthralgia, headache, pain in extremity, and allodynia, were reported by markedly more subjects in the tanezumab treatment group than in the placebo treatment group.