Supplementary Material

Figure S1. Graphical Multiple Testing Procedure for Control of Type 1 Error Rate.

Testing of primary and key secondary end points followed the graphical approach of gatekeeping strategy to control the family-wise type 1 error rate of 5% (2-sided). The graph starts with testing tanezumab 10mg versus placebo for low back pain intensity (LBPI) at week 16 at $\alpha = 0.05$, and if statistically significant ($P \leq 0.05$), $\alpha = 0.05$ is split with equal weight to testing tanezumab 10mg versus placebo for 50% responder at $\alpha = 0.025$, and testing tanezumab 5mg versus placebo for LBPI at week 16 at $\alpha = 0.025$. If the test of tanezumab 10mg versus placebo for 50% responder is significant at $\alpha = 0.025$, additional $\alpha = 0.02$ (0.8*0.025) will be reallocated to the test of tanezumab 5mg versus placebo for LBPI at week 16. Then tanezumab 5mg versus placebo for LBPI at week 16 can be tested at 0.045. This iterative process of updating the graph and reallocating α is repeated until all primary and key secondary end points have been tested or when no remaining hypotheses can be rejected at their corresponding α level. RMDQ denotes Roland Morris Disability Questionnaire.

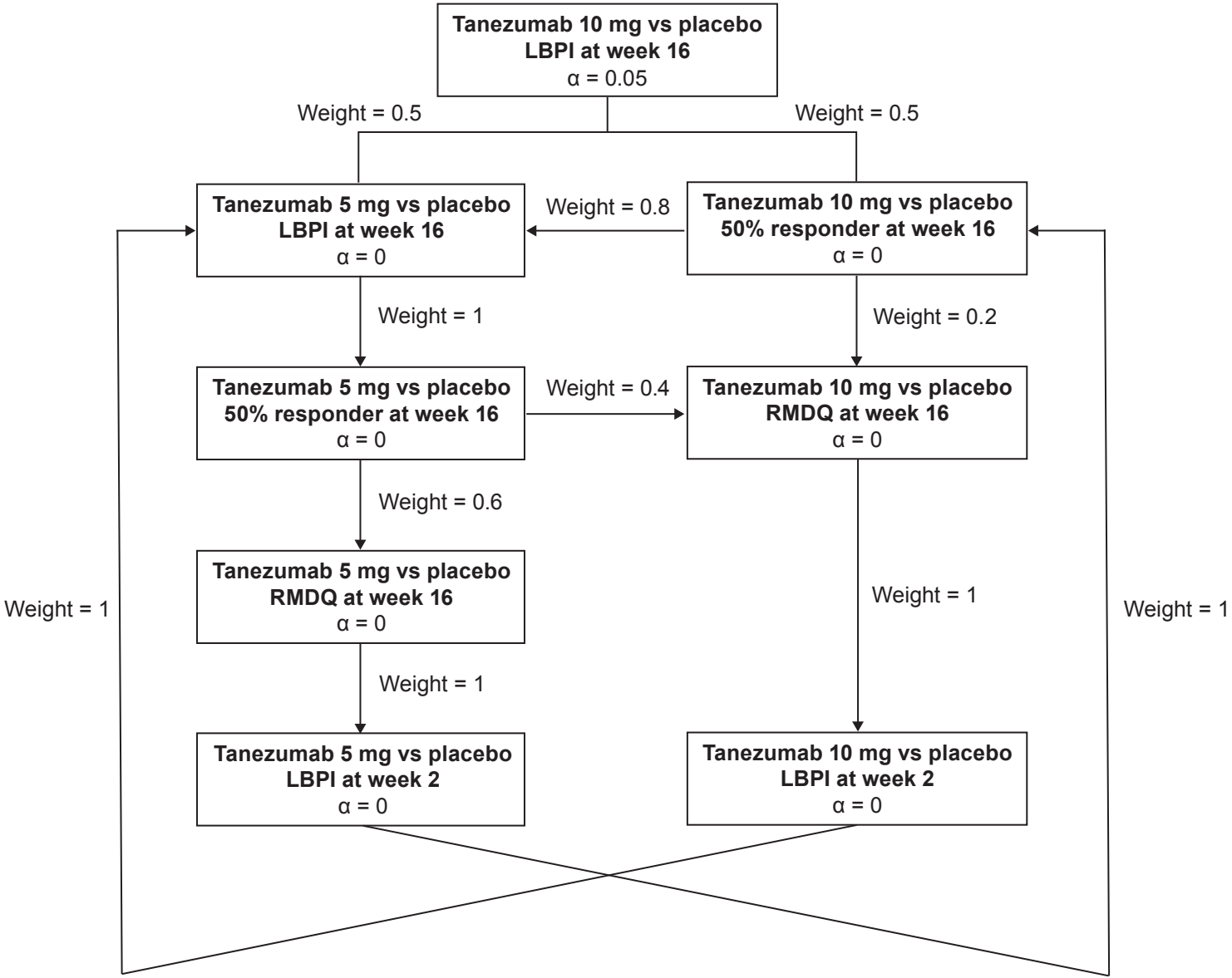
Tanezumab 10 mg vs placebo
LBPI at week 16
α = 0.05
Weight = 0.5
Weight = 0.5
Tanezumab 5 mg vs placebo
LBPI at week 16
α = 0
Weight = 0.8
Tanezumab 10 mg vs placebo
50% responder at week 16
α = 0
Weight = 1
Weight = 0.2
Tanezumab 5 mg vs placebo
50% responder at week 16
α = 0
Weight = 0.4
Tanezumab 10 mg vs placebo
RMDQ at week 16
α = 0
Weight = 0.6
Tanezumab 5 mg vs placebo
RMDQ at week 16
α = 0
Weight = 1
Weight = 1
Weight = 1
Weight = 1
Tanezumab 5 mg vs placebo
LBPI at week 2
α = 0
Tanezumab 10 mg vs placebo
LBPI at week 2
α = 0

Figure S2. Summary of Cumulative Reduction, from Baseline, in LBPI Score at Week 16.

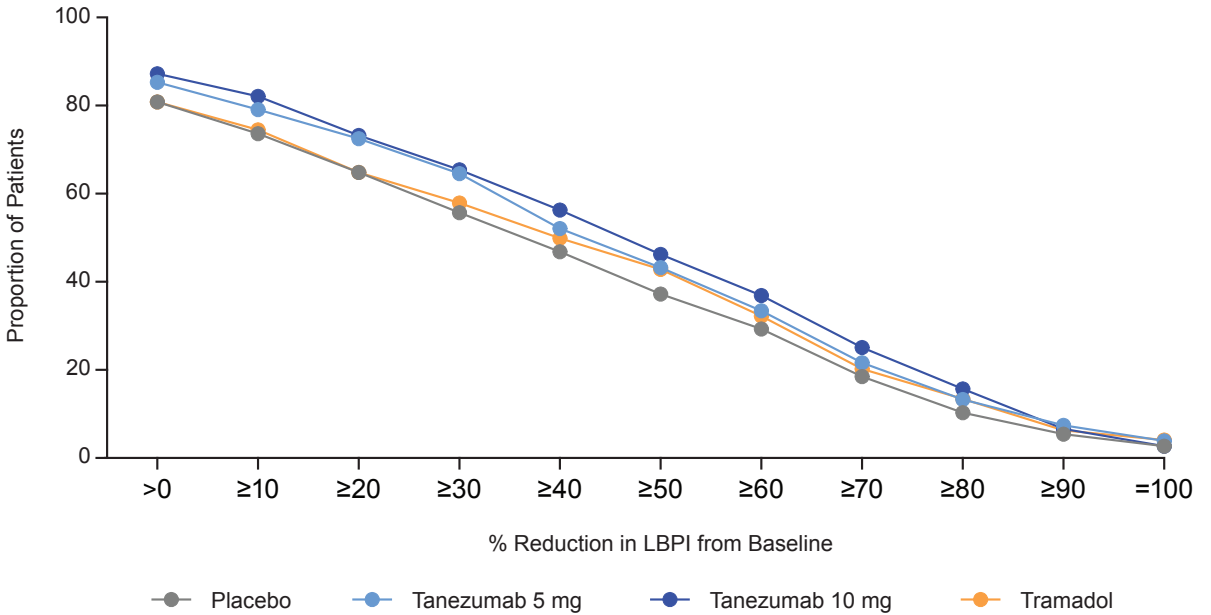

Table S1. Protocol-Qualifying† Prior Drug Treatments for Chronic Low Back Pain in the Safety Population; n (%) of Patients.

	Placebo (n = 215)	Tanezumab 5mg (n = 506)	Tanezumab 10mg (n = 502)	Tramadol (n = 602)
Any prior medication for CLBP	215 (100.0)	506 (100.0)	502 (100.0)	602 (100.0)
Acetaminophen or low-dose NSAIDs	197 (91.6)	458 (90.5)	460 (91.6)	559 (92.9)
Prescription NSAIDs	176 (81.9)	438 (86.6)	440 (87.6)	511 (84.9)
Opioids (not including tramadol)	158 (73.5)	361 (71.3)	341 (67.9)	421 (69.9)
Benzodiazepines and skeletal muscle relaxants	76 (35.3)	193 (38.1)	198 (39.4)	249 (41.4)
Lidocaine patch	37 (17.2)	102 (20.2)	100 (19.9)	110 (18.3)
Duloxetine or other SNRIs	16 (7.4)	33 (6.5)	26 (5.2)	34 (5.6)
Tricyclic antidepressants	8 (3.7)	9 (1.8)	11 (2.2)	19 (3.2)
Tapentadol	4 (1.9)	11 (2.2)	10 (2.0)	15 (2.5)
NSAIDs	0	1 (0.2)	0	0
Received ≥2 of the above categories*	214 (99.5)	506 (100.0)	502 (100.0)	601 (99.8)
Received ≥3 of the above categories*	207 (96.3)	491 (97.0)	487 (97.0)	583 (96.8)
Received ≥4 of the above categories	33 (15.3)	94 (18.6)	83 (16.5)	121 (20.1)
Received ≥5 of the above categories	3 (1.4)	9 (1.8)	10 (2.0)	11 (1.8)
Received ≥6 of the above categories	0	0	2 (0.4)	0

Numbers based on the safety population.

* Despite criteria requiring inadequate response to ≥3 categories, some patients not meeting this criteria were enrolled initially but were withdrawn as a protocol violation.

† Patients were required to have a history of inadequate response and/or intolerance.

CLBP = chronic low back pain; NSAID = nonsteroidal anti-inflammatory drug; SNRI = serotonin–norepinephrine reuptake inhibitor.

Table S2. Summary of Reported Deaths*.

	Placebo/ tanezumab 5mg	Placebo/ tanezumab 10mg	Tanezumab 5mg	Tramadol
During the 56-week treatment period	• Cardiac failure (prior to switch to tanezumab)	• Road traffic accident (after switch to tanezumab at week 16)		• Aspiration and pneumonia
During the 24-week follow-up period	• Aneurysmal rupture and myocardial infarction	• Toxicity to multiple agents (fentanyl, cocaine, and heroin)	• Influenza • Toxicity to fentantyl	

* No deaths were deemed treatment-related by the investigator.