Supplementary Material

Clinical meaningfulness of response to tanezumab in patients with chronic low back pain: Analysis from a 56-week, randomized, placebo- and tramadol-controlled, phase 3 trial

John D. Markman [a],*, Thomas J. Schnitzer [b], Serge Perrot [c], Said R. Beydoun [d], Seiji Ohtori [e], Lars Viktrup [f], Ruoyong Yang [g], Candace Bramson [h], Christine R. West [i], Kenneth M. Verburg [j]

[a] University of Rochester School of Medicine and Dentistry, 2180 S. Clinton Ave, Rochester, NY 14618, USA; John_Markman@URMC.Rochester.edu

[b] Northwestern University Feinberg School of Medicine, 710 N Lake Shore Drive, Room 1020, Chicago, IL 60611, USA; tjs@northwestern.edu

[c] Pain Center, Cochin Hospital, INSERM U 987, Paris University, Paris, France; serge.perrot@aphp.fr

[d] University of Southern California, 1520 San Pablo Street, Suite 3000, Los Angeles, CA 90033 USA; sbeydoun@usc.edu

[e] Chiba University, 1-8-1 Inohana, Chuo-ku, Chiba, 260-8670 Japan; sohtori@faculty.chiba-u.jp

[f] Eli Lilly & Company, 893 Delaware St, Indianapolis, IN 46225 USA; viktrup_lars@lilly.com

[g] Pfizer Inc, 235 E 42nd St, New York, NY 10017, USA; Ruoyong.Yang@pfizer.com

[h] Pfizer Inc, 445 Eastern Point Road, Groton, CT 06340, USA; Candace.Bramson@pfizer.com

[i] Pfizer Inc, 445 Eastern Point Road, Groton, CT 06340, USA; Christine.West@pfizer.com

[j] Pfizer Inc, 445 Eastern Point Road, Groton, CT 06340, USA; Kenneth.M.Verburg@pfizer.com

Corresponding author: E-mail address: John_Markman@URMC.Rochester.edu (J.D. Markman).

Table of contents

Supplementary Table 1. Change from baseline in LBPI and RMDQ scores at week 16 and week 56.[a,b]

	Placebo (N=406)	Tanezumab 5 mg (N=407)	Tanezumab 10 mg (N=407)	Tramadol (N=605)
Week 16 LBPI				
Mean (SD) score at baseline[c]	7.19 (1.12)	7.24 (1.08)	7.18 (1.13)	7.17 (1.16)
LS mean (SE) change from baseline	−2.68 (0.15)	−2.98 (0.14)	−3.08 (0.14)	−2.81 (0.12)
LS mean (SE) difference vs placebo	-	−0.30 (0.19)	−0.40 (0.18)	−0.12 (0.17)
p-value vs placebo	-	0.1117	0.0281	0.4620
LS mean (SE) difference vs tramadol	-	−0.17 (0.17)	−0.28 (0.17)	-
p-value vs tramadol	-	0.3118	0.0958	-
Week 16 RMDQ				
Mean (SD) score at baseline[d]	14.81 (5.14)	15.02 (5.21)	15.06 (4.92)	15.10 (5.11)
LS mean (SE) change from baseline	−4.95 (0.36)	−6.27 (0.35)	−6.69 (0.35)	−5.21 (0.30)
LS mean (SE) difference vs placebo	-	−1.32 (0.45)	−1.74 (0.46)	−0.26 (0.42)
p-value vs placebo	-	0.0035	0.0002	0.5412
LS mean (SE) difference vs tramadol	-	−1.06 (0.42)	−1.48 (0.42)	-
p-value vs tramadol	-	0.0107	0.0004	-
Week 56 LBPI				
LS mean (SE) change from baseline	-	−2.52 (0.17)	−2.62 (0.17)	−2.40 (0.15)
LS mean (SE) difference vs tramadol	-	−0.11 (0.20)	−0.21 (0.20)	-
p-value vs tramadol	-	0.5763	0.2887	-
Week 56 RMDQ	-			
LS mean (SE) change from baseline	-	−4.85 (0.45)	−5.23 (0.44)	−4.41 (0.36)
LS mean (SE) difference vs tramadol	-	−0.44 (0.52)	−0.83 (0.52)	-
p-value vs tramadol	-	0.3981	0.1089	-

[a] LBPI scores range from 0 to 10 and RMDQ scores range from 0 to 24; negative values represent an improvement in pain, disability, and disease status, respectively.

[b] These results have been disclosed previously in the primary publication (Markman JD, et al. Pain. 2020;161(9): 2068-78).

[c] Baseline n is 404, 406, 406, and 605 for placebo, tanezumab 5 mg, tanezumab 10 mg, and tramadol, respectively.

[d] Baseline n is 406, 405, 407, and 605 for placebo, tanezumab 5 mg, tanezumab 10 mg, and tramadol, respectively.

LBPI, low back pain intensity; LS, least-squares; RMDQ, Roland Morris Disability Questionnaire; SD, standard deviation; SE, standard error.

Supplementary Table 2. List of IECs or IRBs approving the study protocol.

Schulman Associates IRB 4445 Lake Forest Dr, Ste 300 Cincinnati, OH 45242 UNITED STATES
Western Institutional Review Board 1019 39th Ave SE, Ste 120 Puyallup, WA 98374-2115 UNITED STATES
Advarra IRB 6940 Columbia Gateway Dr, Ste 110 Columbia, MD 21046 UNITED STATES
Partners Human Research Committee 399 Revolution Dr, Ste 710 Somerville, MA 02145 UNITED STATES
USC Health Sciences Institutional Review Board 1200 N State St, Ste 4700 Los Angeles, CA 90033 UNITED STATES
Human Subjects Research Office 1400 NW 10th Ave, 12th Fl (M809) Ste 1200A Miami, FL 33136 UNITED STATES
Northwestern University Institutional Review Board 750 N Lake Shore Dr Chicago, IL 60611 UNITED STATES
De Videnskabsetiske Komiteer for Region Syddanmark Regionshuset, Damhaven12, Vejle, 7100 DENMARK
Comite de Protection des Personnes 9 avenue Charles de GaulleIle-de-France VIII, Hopital Ambroise Pare Boulogne Billancourt, 92100 FRANCE
Egeszsegugyi Tudomanyos Tanacs Klinikai Farmakologiai Etikai Bizottsaga Arany Janos. u. 6-8 Budapest, 1051 HUNGARY

Local Incorporated Administrative Agency Rinku General Medical Center Institutional Review Board
2-23, RinkuOuraikita
Izumisano, OSAKA 598-8577
JAPAN

IRB of All Tohoku Clinical Trial Review and Audit Organization
1-6-10, Kamisugi, Aoba-ku
Sendai, MIYAGI 980-0011
JAPAN

SHINAGAWA EAST ONE MEDICAL CLINIC IRB
2-16-1, Konan, Shinagawa East One Tower 3F
Minato-ku, TOKYO 108-0075
JAPAN

IRB of Funabashi municipal Medical Center
1-21-1, Kanasugi
Funabashi, CHIBA 273-8588
JAPAN

National Hospital Organization Central Review Board
2-5-21, Higashigaoka
Meguro-ku, TOKYO 152-0021
JAPAN

Drug Acceptance Research Review Board of Toyama University Hospital
2630 Sugitani
Toyama, TOYAMA 930-0194
JAPAN

Medical Corporation Koyukai Nishi Hospital IRB
3-2-18 Bingo-Cho, Nada
Kobe, HYOGO 657-0037
JAPAN

Medical corporate corporation hoshikai Onishi medical clinic IRB
2-9-1,Kunioka Inami-cho
Kako-gun, HYOGO 675-1115
JAPAN

MARUNOUCHI HOSPITAL INSTITUTIONAL REVIEW BOARD
1-7-45, Nagisa
Matsumoto, NAGANO 390-8601
JAPAN

Chiba Rosai Hospital Institutional Review Board
2-16, Tatsumidai-Higashi
Ichihara, CHIBA 290-0003
JAPAN

Adachikyousai Hospital Institutional Review Board
1-36-8 Yanagihara
Adachi, TOKYO 120-0022

JAPAN

Kobe Red Cross Hospital Institutional Review Board
1-3-1 Wakinohamakaigandori, Chuo-ku
Kobe, HYOGO 651-0073
JAPAN

IRB of All Tohoku Clinical Trial Review and Audit Organization
1-6-10, Kamisugi, Aoba-ku
Sendai, MIYAGI 980-0011
JAPAN

Hamamatsu university school of medicine, University hospital Institutional Review Board
1-20-1 Handayama, Higashi-ku
Hamamatsu, SHIZUOKA 431-3192
JAPAN

Chiba Central Medical Center IRB
1835-1, Kasoricho, Wakaba-ku
Chiba, CHIBA 264-0017
JAPAN

Saiseikai Central Hospital IRB
1-4-17, Mita
Minato-ku, TOKYO 108-0073
JAPAN

Medical Co. Keiaikai Saga Memorial Hospital Institutional Review Board
1240-1,oaza-Nagase,Takakise-machi
Saga, SAGA 849-0917
JAPAN

Fukui General Hospital Institutional Review Board
58-16-1 Egami-cho,
Fukui, FUKUI 910-3113
JAPAN

Yamaguchi University Hospital Institutional Review Board
1-1-1, Minami-Kogushi
Ube, YAMAGUCHI 755-8505
JAPAN

Haradoi Hospital Institutional Review Board
6-40-8, Aoba, Higashi-ku
Fukuoka, FUKUOKA 813-8588
JAPAN

Jinbo Orthopedics Clinical Institutional Review Board
5-38-41, Honcho
Koganei, TOKYO 184-0004
JAPAN

Keio University Hospital IRB
35, Shinano-machi

Shinjuku-ku, TOKYO 160-8582
JAPAN

Yonezawa City Hospital Institutional Review Board
6-36, Aioi-cho
Yonezawa, YAMAGATA 992-8502
JAPAN

Hiroshima Red Cross Hospital & Atomic-bomb Survivors Hospital Institutional Review Board
1-9-6, Senda-machi,Naka-ku
Hiroshima, HIROSHIMA 730-8619
JAPAN

Institutional Review Board of International Health and Welfare Group of Kyushu district
3-6-45, Momochihama, Sawara-ku
Fukuoka, FUKUOKA 814-0001
JAPAN

Chiba University Hospital Institutional Review Board
1-8-1 Inohana, Chuo-ku
Chiba, CHIBA 260-8677
JAPAN

Saitama Municipal Hospital Institutional Review Board
2460 Mimuro, Midori-ku
Saitama, SAITAMA 336-8522
JAPAN

Sakayori Clinic IRB
2-26-3, Higashioi
Shinagawa-ku, TOKYO 140-0011
JAPAN

Sapporo City General Hospital IRB
13-1-1, Kita11jonishi, Chuo-ku
Sapporo, HOKKAIDO 060-8604
JAPAN

Nagoya University Hospital IRB
Tsurumai-cho, Showa-ku, 65
Nagoya, AICHI 466-8560
JAPAN

Shimonoseki City Hospital IRB
1-13-1, Koyo-cho
Shimonoseki-shi, YAMAGUCHI 750-8520
JAPAN

Minamiosaka Hospital IRB
1-18-18, Higashikagaya
Suminoe-ku, Osaka, OSAKA 559-0012
JAPAN

Aichi Medical University Hospital IRB

1-1 Yazakokarimata
Nagakute, AICHI 480-1195
JAPAN

Hayashi Diabetes Clinic IRB
3-2, Shinei-cho, Abeasa Medical 2F
Chigasaki, KANAGAWA 253-0044
JAPAN

Toyooka Chuo Hospital Institutional Review Board
2-1-5 Toyooka 7jo
Asahikawa, HOKKAIDO 078-8237
JAPAN

Tokyo Medical and Dental University Medical Hospital IRB
1-5-45 Yushima
Bunkyo-ku, TOKYO 113-8519
JAPAN

Kyushu Rosai Hospital IRB
1-1 Sonekitamachi, Kokuraminami-ku,
Kitakyushu, FUKUOKA 800-0296
JAPAN

Jimbo Orthopedics IRB
5-38-41, Honcho
Koganei, TOKYO 184-0004
JAPAN

Hakodate Central General Hospital IRB
Honcho, 33-2
Hakodate, HOKKAIDO 040-8585
JAPAN

Institutional Review Board of Seoul National University Hospital
101 Daehak-ro, Jongno-gu
Seoul, KOREA 03080
REPUBLIC OF KOREA

Institutional Review Board of KyungHee University Hospital
23, Kyungheedae-ro, Dongdaemun-gu
Seoul, 02447
REPUBLIC OF KOREA

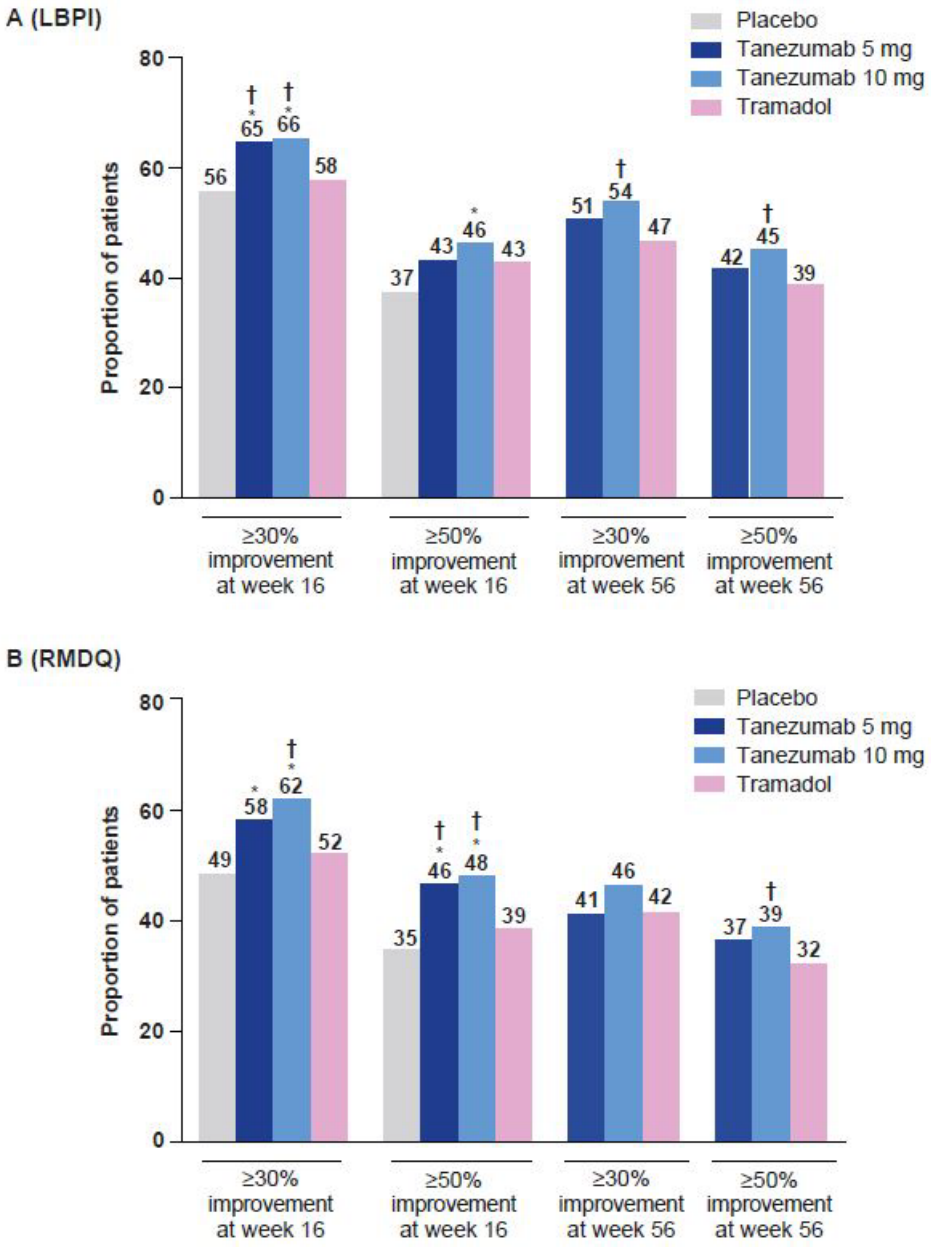
Institutional Review Board, Severance Hospital, Yonsei University Health System
50-1 Yonsei-ro, Seodaemun-gu
Seoul, 03722
REPUBLIC OF KOREA

IRB of Samsung Medical Center
81 Irwon-ro, Gangnam-gu
Seoul, 06351
REPUBLIC OF KOREA

Institutional Review Board / Institutional Ethics Committee of Korea University Guro Hospital 148 Gurodong-ro, Guro-gu Seoul, 152-703 (08308) KOREA, REPUBLIC OF
Comite etico Investigacion Clinica Grupo Hospitalario Quiron en Barcelona Sede de Gestion. Fundacion Teknon, C/ Vilana, 12 Barcelona, BARCELONA 08022 SPAIN
Regionala Etikprovningsnamnden i Goteborg Guldhedsgatan 5 A Goteborg, 413 20 SWEDEN
Etikprövningsmyndigheten Box 2110 Uppsala, 750 02 SWEDEN

IEC, independent ethics committee; IRB, institutional review board

Supplementary Figure 1. Proportion of patients with ≥30% and ≥50% improvement from baseline in LBPI (A) and RMDQ (B) at week 16 and week 56.[a]



*p≤0.05 vs placebo; †p≤0.05 vs tramadol.

[a] 30% and 50% improvement in LBPI at week 16 (tanezumab versus placebo; tramadol versus placebo) results have been disclosed previously in the primary publication (Markman JD, et al. Pain. 2020;161(9):2068-78).

LBPI, low back pain intensity; RMDQ, Roland Morris Disability Questionnaire.