Supporting Online Material

Tanenberg RJ, Irving GA, Risser RC, Ahl J, Robinson MJ, Skljarevski V, Malcom SK. Duloxetine, Pregabalin, and Duloxetine Plus Gabapentin for Diabetic Peripheral Neuropathic Pain Management in Patients With Inadequate Pain Response to Gabapentin: An Open-Label, Randomized, Noninferiority Comparison. *Mayo Clin Proc*. 2011;86(7):615-624.

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This supplementary material has been peer reviewed and the authors confirm that data are accurate.

TABLE S1. **Concomitant Use of TCAs and Opioids During the Study**

Variable	Group 1 Pregabalin (n=134)	Group 2 Duloxetine + gabapentin (n=135)	Group 3 Duloxetine (n=138)	P values 1 vs 2	P values 1 vs 3	P values 2 vs 3
Any TCA	22 (16.4)	5 (3.7)	11 (8.0)	<.001	.04	.20
Amitriptyline	17 (12.7)	5 (3.7)	9 (6.5)	.01	>.99	.41
Doxepin	3 (2.2)	0	0	.12	.12	NA
Nortriptyline	1 (0.7)	0	2 (1.4)	.50	>.99	.50
Opipramol	1 (0.7)	0	0	.50	.49	NA
Any opioid	17 (12.7)	21 (15.6)	19 (13.8)	.60	.86	.73
Hydrocodone bitartrate–acetaminophen	4 (3.0)	4 (3.0)	11 (8.0)	>.99	.11	.11
Hydrocodone	6 (4.5)	4 (3.0)	2 (1.4)	.54	.17	.44
Propoxyphene	4 (3.0)	2 (1.5)	1 (0.7)	.45	.21	.62
Tramadol	0	4 (3.0)	2 (1.4)	.25	.50	.68
Paracetamol-codeine	2 (1.5)	2 (1.5)	0	>.99	.24	.24
Dextropropoxyphene	0	2 (1.5)	1 (0.7)	.50	>.99	.62
Morphine	0	1 (0.7)	2 (1.4)	>.99	.50	>.99
Oxycodone	0	2 (1.5)	1 (0.7)	.50	>.99	.62
Oxycodone-acetaminophen	1 (0.8)	0	1 (0.7)	.50	>.99	>.99
Pethidine	0	1 (0.7)	1 (0.7)	>.99	>.99	>.99
Methadone	0	1 (0.7)	0	>.99	NA	.50
Paracetamol-tramadol	1 (0.8)	0	0	.50	.49	NA
Tilidine	0	1 (0.7)	0	>.99	NA	.50

Data are provided as number (percentage) of patients. *P* values are from the Fisher exact test. NA = not applicable; TCA = tricyclic antidepressant.

TABLE S2. **Per-Protocol Population and Reasons for Exclusion[a]**

Variable	Pregabalin	Duloxetine + gabapentin	Duloxetine
Per-protocol population	97/134 (72.4)	105/135 (77.8)	79/138 (57.2)
Excluded from per-protocol group	37/134 (27.6)	30/135 (22.2)	59/138 (42.8)[b]
Reasons for exclusions			
Nonadherence to study drug therapy	35/37 (94.6)	30/30 (100)	55/59 (93.2)
MNSI score <3 at entry	2/37 (5.4)	0	3/59 (5.1)
Gabapentin taper ≥14 d	1/37 (2.7)	0	2/59 (3.4)
Use of prohibited medication	2/37 (5.4)	0	1/59 (1.7)
HbA$_{1c}$ level >12% after randomization	0	0	1/59 (1.7)

[a] Data are provided as number (percentage) of patients. HbA$_{1c}$ = glycated hemoglobin; MNSI = Michigan Neuropathy Screening Instrument.
[b] Significantly greater than pregabalin (*P*=.02) and duloxetine + gabapentin (*P*=.01).

TABLE S3. **Noninferiority[a] Results in Intent-To-Treat and Per-Protocol Patient Populations**

Population	Analysis	Mean difference (95% CI)
	Duloxetine vs pregabalin	
Intent-to-Treat	MMRM[b]	0.49 (–0.05 to 1.04)
	LOCF	0.46 (–0.06 to 0.98)
	BOCF	–0.09 (–0.58 to 0.39)
Per-Protocol	MMRM	0.46 (–0.20 to 1.13)
	LOCF	0.42 (–0.24 to 1.07)
	BOCF	–0.08 (–0.71 to 0.54)
	Duloxetine vs duloxetine + gabapentin	
Intent-to-Treat	MMRM[c]	0.23 (–0.32 to 0.78)
	LOCF	0.15 (–0.37 to 0.68)
	BOCF	–0.25 (–0.74 to 0.23)
Per-Protocol	MMRM	0.18 (–0.49 to 0.85)
	LOCF	0.29 (–0.36 to 0.93)
	BOCF	–0.08 (–0.68 to 0.53)

[a] The prespecified and fixed margin of inferiority (MoNI) of –0.80 was used for each comparison. Except for the primary and secondary objectives specified, all of the results are secondary analyses. Baseline observation carried forward (BOCF) was post hoc. CI = confidence interval; LOCF = last observation carried forward; MMRM = mixed model repeated measures.
[b] Primary objective.
[c] Secondary objective.

TABLE S4. **Subgroup Analysis of Mean Changes in Daily Pain at End Point in Patients Who Did or Did Not Use Concomitant Antidepressants or Pain Medications**

Variable	Group 1 Pregabalin		Group 2 Duloxetine + gabapentin		Group 3 Duloxetine		P values			Test of 3-way interaction
	No.	Mean ± SD	No.	Mean ± SD	No.	Mean ± SD	1 vs 2	1 vs 3	2 vs 3	P value
Antidepressant user	27	–2.3±0.4	13	–2.2±0.5	17	–2.1±0.5	.79	.75	.97	.04
Antidepressant nonuser	66	–2.1±0.2	73	–2.4±0.2	60	–2.8±0.2	.22	.03	.31	
Pain medication user	64	–2.1±0.2	49	–2.5±0.3	51	–2.8±0.3	.27	.03	.31	.70
Pain medication nonuser	29	–2.2±0.3	37	–2.3±0.3	26	–2.2±0.4	.78	.94	.84	
Opioid user	11	–1.3 ±0.6	15	–2.2±0.5	13	–1.9±0.5	.23	.43	.69	.36
Opioid nonuser	82	–2.3±0.2	71	–2.4±0.2	64	–2.8±0.2	.51	.09	.30	
Tricyclic antidepressant user	19	–1.8±0.5	3	–2.7±1.2	7	–2.5±0.7	.48	.41	.90	.52
Tricyclic antidepressant nonuser	74	–2.2±0.2	83	–2.4±0.2	70	–2.6±0.2	.51	.14	.39	