

**Additional Table 4 | Response to PXT3003 on efficacy outcomes (Full Analysis Set, *n* = 80).** Data are mean (s.d.) baseline and final values, and % (s.d.) of improvement for each treatment group and PLI. Differences between treatment groups were assessed by Analysis of Covariance (Ancova) on log-transformed values by adjusting for baseline values. Estimates were provided as mean percentage change over baseline (90% CI). Dose-effect was tested through Spearman’s rank correlation. *P*-values are one-tailed. CMTNS = Charcot-Marie-Tooth Neuropathy Score; ONLS = Overall Neuropathy Limitations Scale; 6MWT = 6-Minute Walk Test; 9HPT = 9-Hole Peg Test; CMAP = Amplitudes of Compound Muscle Action Potentials; MCV = Motor Conduction Velocity; DML = Distal Motor Latency; SNAP = Amplitudes of Sensory Nerve Action Potentials; SCV = Sensitive Conduction Velocity; VAS = Visual Analog Scale; CGI = Clinical Global Impression.

	Placebo ( <i>n</i> = 19)			PXT3003 LD ( <i>n</i> = 21)			PXT3003 ID ( <i>n</i> = 21)			PXT3003 HD ( <i>n</i> = 19)		
	Baseline	Final	% Improvement	Baseline	Final	% Improvement	Baseline	Final	% Improvement	Baseline	Final	% Improvement
CMTNS	14.3 (3.8)	14.2 (3.8)	2.6 (17.5)	14.2 (4.1)	14.5 (4.2)	0.5 (23.2)	13.0 (4.0)	13.5 (3.7)	-3.1 (16.0)	13.8 (3.4)	13.2 (3.9)	7.7 (18.4)
CMTES	9.5 (3.0)	9.4 (2.7)	3.8 (25.1)	9.5 (3.4)	9.9 (3.3)	-2.1 (25.0)	8.8 (2.9)	9.1 (3.1)	-2.0 (20.0)	8.8 (2.7)	8.5 (2.7)	6.8 (21.8)
CMTNS: Sensory Symptoms	1.8 (1.1)	1.6 (0.8)	26.3 (87.2)	2.1 (1.1)	2.1 (1.2)	19.4 (84.2)	1.5 (0.7)	1.6 (0.7)	-0.8 (29.1)	1.7 (0.8)	1.4 (0.6)	36.0 (79.0)
CMTNS: Motor Symptoms: Legs	2.4 (0.8)	2.3 (0.7)	5.3 (15.8)	2.3 (0.6)	2.3 (0.7)	4.0 (26.8)	2.2 (0.8)	2.1 (0.9)	17.5 (41.7)	2.1 (0.5)	2.1 (0.5)	0.0 (0.0)
CMTNS: Motor Symptoms: Arms	1.7 (0.8)	1.6 (0.6)	5.3 (22.9)	1.9 (0.6)	1.8 (0.5)	4.8 (26.9)	1.8 (0.5)	1.7 (0.6)	11.9 (38.4)	1.7 (0.6)	1.6 (0.6)	5.3 (22.9)
CMTNS: Pin Sensitivity	2.5 (1.0)	2.4 (0.8)	10.5 (55.3)	2.3 (1.0)	2.1 (0.9)	27.8 (78.2)	2.4 (1.1)	2.6 (0.9)	-3.6 (35.4)	2.2 (0.9)	2.1 (0.9)	21.9 (74.3)
CMTNS: Vibration Sensitivity	2.8 (0.9)	3.3 (1.3)	-4.7 (35.2)	2.8 (1.0)	3.3 (1.2)	-11.2 (28.7)	2.7 (1.2)	3.2 (1.1)	-11.1 (38.4)	2.7 (0.7)	3.0 (1.0)	-3.2 (27.0)
CMTNS: Strength: Legs	2.7 (0.7)	2.6 (0.7)	5.3 (19.3)	2.6 (0.8)	2.6 (0.7)	0.0 (21.9)	2.6 (0.7)	2.6 (0.7)	0.8 (13.4)	2.8 (1.0)	2.6 (0.9)	9.2 (19.0)
CMTNS: Strength: Arms	2.5 (0.6)	2.6 (0.6)	0.0 (21.5)	2.6 (0.9)	2.7 (0.7)	-0.4 (30.1)	2.4 (0.9)	2.3 (0.8)	4.4 (18.9)	2.6 (1.1)	2.7 (0.8)	-3.9 (20.5)
CMTNS: CMAP	2.7 (0.9)	2.6 (1.0)	7.9 (27.4)	2.7 (0.9)	2.6 (0.8)	6.3 (37.7)	2.4 (1.0)	2.2 (0.9)	11.9 (30.8)	2.8 (1.0)	2.6 (0.9)	8.8 (24.4)
CMTNS: SNAP	4.1 (1.3)	4.2 (1.2)	-2.1 (20.8)	4.0 (1.2)	4.0 (1.4)	13.8 (53.6)	3.9 (1.4)	4.1 (1.3)	-1.0 (42.1)	4.2 (1.1)	4.1 (1.0)	4.1 (28.5)
ONLS	3.1 (1.1)	3.3 (0.9)	-5.3 (19.3)	3.3 (1.0)	3.6 (0.9)	-6.5 (18.5)	3.5 (0.9)	3.4 (0.9)	4.8 (24.2)	3.6 (0.8)	3.4 (1.0)	12.3 (28.4)
ONLS: Arm	2.4 (0.8)	2.4 (0.8)	3.5 (18.1)	2.7 (0.7)	2.9 (0.7)	-4.4 (11.1)	2.7 (0.7)	2.7 (0.7)	7.1 (45.5)	2.7 (0.7)	2.5 (0.8)	20.2 (37.9)
ONLS: Leg	2.7 (0.5)	2.9 (0.3)	-7.0 (14.0)	2.6 (0.5)	2.8 (0.4)	-4.0 (18.2)	2.8 (0.4)	2.7 (0.5)	2.4 (10.9)	2.8 (0.4)	2.9 (0.3)	-1.8 (7.6)
6MWT (m)	468.2 (99.9)	509.2 (107.7)	9.0 (8.3)	473.1 (70.9)	500.9 (75.7)	6.2 (8.3)	450.7 (71.1)	481.4 (95.2)	6.4 (9.4)	429.3 (83.7)	472.0 (98.0)	9.9 (6.9)
9HPT (s)	17.2 (2.5)	16.6 (3.0)	4.9 (11.4)	16.1 (3.9)	16.3 (3.5)	-1.2 (11.7)	18.4 (4.7)	17.4 (3.8)	5.6 (9.9)	20.8 (7.8)	19.1 (5.9)	7.8 (12.1)
Ankle Dorsiflexion (Nm)	7.8 (6.6)	7.4 (5.6)	20.2 (88.4)	9.1 (5.0)	7.7 (3.6)	-3.6 (43.0)	8.3 (5.6)	8.3 (5.1)	81.5 (369.6)	8.2 (6.1)	7.9 (5.2)	20.4 (64.1)
Grip (kg)	22.6 (10.7)	24.5 (12.0)	9.9 (24.2)	21.6 (6.1)	22.1 (7.8)	1.3 (15.6)	23.1 (9.2)	24.0 (9.3)	4.7 (12.5)	20.6 (10.4)	22.4 (10.3)	11.7 (18.1)
CMAP (milliV)	3.7 (2.0)	4.4 (2.0)	34.4 (62.0)	4.0 (1.8)	3.5 (1.7)	1.4 (38.7)	3.7 (2.1)	4.0 (2.2)	22.9 (62.6)	3.4 (2.3)	3.9 (2.1)	64.2 (208.5)
MCV (m/s)	21.5 (3.6)	22.4 (4.7)	3.7 (8.5)	22.7 (4.7)	22.5 (5.6)	3.0 (11.5)	20.8 (4.8)	21.6 (3.8)	5.7 (12.3)	20.5 (5.3)	21.6 (4.8)	9.0 (17.6)
DML (ms)	8.6 (2.2)	8.6 (2.3)	0.4 (8.8)	7.9 (2.1)	7.9 (2.0)	3.6 (21.7)	8.2 (1.8)	7.3 (1.3)	15.3 (35.8)	8.2 (1.9)	7.6 (1.4)	8.4 (21.7)
SNAP (microV)	2.6 (3.2)	2.6 (2.9)	12.4 (121.7)	2.3 (3.0)	3.0 (3.7)	11.5 (88.2)	2.6 (3.8)	2.8 (3.6)	23.3 (128.4)	2.2 (2.7)	2.5 (2.7)	5.2 (69.0)
SCV (m/s)	31.1 (14.8)	31.3 (12.1)	3.4 (11.0)	29.4 (8.2)	30.9 (7.5)	5.3 (11.2)	31.3 (9.4)	33.9 (9.1)	29.5 (63.4)	29.9 (7.7)	35.8 (10.4)	30.5 (10.0)
VAS: Pain	83.9 (23.1)	80.8 (21.2)	0.8 (32.0)	85.6 (16.8)	70.9 (23.7)	-16.7 (23.4)	82.0 (17.5)	84.3 (16.7)	9.1 (41.3)	80.9 (22.2)	71.1 (24.0)	-6.7 (44.3)
VAS: Fatigue	61.6 (27.4)	65.8 (26.3)	29.8 (80.3)	70.0 (20.8)	57.1 (26.1)	-17.4 (33.7)	70.2 (18.6)	61.2 (22.3)	-6.8 (40.5)	62.6 (29.6)	57.3 (26.4)	-1.0 (39.7)
VAS: Global	65.5 (25.3)	74.7 (18.6)	51.3 (152.4)	72.5 (18.9)	71.4 (18.5)	1.8 (27.8)	64.4 (27.5)	71.4 (21.2)	62.3 (161.6)	78.4 (16.5)	70.8 (19.8)	-8.1 (26.3)
CGI: Global Improvement	4.0 (0.0)	4.1 (0.2)	-1.1 (4.6)	4.0 (0.0)	4.0 (0.3)	0.6 (8.7)	4.0 (0.0)	3.7 (0.5)	9.5 (15.4)	4.0 (0.0)	4.1 (0.3)	-2.1 (6.3)
CGI: Illness Severity	3.5 (1.1)	3.4 (1.1)	5.9 (27.6)	3.5 (0.8)	3.5 (0.9)	12.7 (68.0)	3.5 (0.7)	3.7 (1.1)	-1.7 (23.9)	3.7 (0.9)	3.8 (0.9)	-2.6 (16.4)
CGI: Therapeutic Effect	4.0 (0.0)	3.9 (0.2)	1.8 (7.6)	4.0 (0.0)	4.0 (0.2)	1.6 (7.3)	4.0 (0.0)	3.7 (0.6)	12.7 (24.7)	4.0 (0.0)	4.0 (0.0)	0.0 (0.0)

	PLI (n = 61)		PXT3003 LD versus Placebo		PXT3003 ID versus Placebo		PXT3003 HD versus Placebo		PXT3003 HD versus PLI		Dose-effect		
	Baseline	Final	% Improvement	Estimate	P-value	Estimate	P-value	Estimate	P-value	Estimate	P-value	Correlation	P-value
<b>CMTNS</b>	13.9 (4.0)	14.0 (3.9)	-0.1 (19.0)	-2.6 (-11.9;7.6)	0.67	-3.1 (-11.0;5.4)	0.74	5.5 (-3.4;15.2)	0.16	8.0 (0.4;16.2)	0.042	0.06	0.3
<b>CMTES</b>	9.3 (3.1)	9.5 (3.0)	-0.2 (23.2)	-4.9 (-15.4;6.9)	0.76	-1.9 (-12.1;9.4)	0.62	6.3 (-5.3;19.2)	0.19	8.7 (-0.39;18.6)	0.058	0.034	0.38
<b>CMTNS: Sensory Symptoms</b>	1.8 (1.0)	1.8 (1.0)	14.6 (71.1)	-13.0 (-31.8;10.9)	0.83	-6.6 (-23.7;14.2)	0.72	14.0 (-8.1;41.3)	0.16	21.0 (1.4;44.3)	0.038	0.081	0.24
<b>CMTNS: Motor Symptoms: Legs</b>	2.3 (0.7)	2.2 (0.8)	9.0 (30.5)	-2.6 (-11.6;7.3)	0.68	7.4 (-5.5;22.1)	0.18	-3.3 (-8.0;1.7)	0.87	-5.3 (-13.4;3.6)	0.84	-0.038	0.63
<b>CMTNS: Motor Symptoms: Arms</b>	1.8 (0.6)	1.7 (0.6)	7.4 (30.1)	-5.1 (-15.1;6.2)	0.78	-0.1 (-12.6;14.2)	0.51	-0.007 (-9.5;10.5)	0.5	1.1 (-8.2;11.4)	0.42	-0.02	0.57
<b>CMTNS: Pin Sensitivity</b>	2.4 (1.0)	2.4 (0.9)	11.6 (59.6)	18.1 (-3.9;45.2)	0.091	-6.4 (-20.6;10.4)	0.75	15.3 (-6.3;42.0)	0.13	9.4 (-7.5;29.4)	0.19	-0.056	0.69
<b>CMTNS: Vibration Sensitivity</b>	2.8 (1.0)	3.3 (1.2)	-9.2 (33.9)	-5.1 (-20.6;13.5)	0.69	-3.8 (-19.4;14.8)	0.64	4.8 (-12.2;25.1)	0.33	8.6 (-5.3;24.4)	0.16	0.017	0.44
<b>CMTNS: Strength: Legs</b>	2.6 (0.8)	2.6 (0.7)	1.9 (18.3)	-3.7 (-12.8;6.2)	0.74	-2.8 (-10.1;5.2)	0.73	3.6 (-5.0;13.0)	0.25	6.1 (-1.2;13.9)	0.084	0.085	0.23
<b>CMTNS: Strength: Arms</b>	2.5 (0.8)	2.5 (0.7)	1.4 (23.8)	-2.4 (-14.2;11.0)	0.63	7.1 (-3.0;18.2)	0.12	-3.6 (-12.5;6.2)	0.73	-5.5 (-14.0;3.8)	0.84	0.012	0.46
<b>CMTNS: CMAP</b>	2.6 (0.9)	2.5 (0.9)	8.7 (32.0)	-3.5 (-16.4;11.4)	0.66	4.8 (-7.9;19.1)	0.27	0.2 (-11.1;13.0)	0.49	-0.8 (-11.0;10.7)	0.55	0.089	0.22
<b>CMTNS: SNAP</b>	4.0 (1.3)	4.1 (1.3)	3.7 (41.6)	9.9 (-7.1;30.0)	0.17	-1.4 (-16.7;16.7)	0.56	3.2 (-8.3;16.1)	0.33	0.7 (-12.5;15.9)	0.47	0.024	0.42
<b>ONLS</b>	3.3 (1.0)	3.4 (0.9)	-2.2 (21.2)	-3.9 (-14.2;7.6)	0.72	6.9 (-3.8;18.8)	0.15	14.4 (0.55;30.2)	0.043	12.1 (2.0;23.2)	0.024	0.28	0.0059
<b>ONLS: Arm</b>	2.6 (0.8)	2.6 (0.8)	2.0 (29.2)	-8.1 (-15.2;-0.41)	0.96	-2.8 (-14.2;10.2)	0.65	13.7 (0.22;29.0)	0.047	15.7 (4.9;27.6)	0.0076	0.22	0.027
<b>ONLS: Leg</b>	2.7 (0.5)	2.8 (0.4)	-2.7 (15.0)	4.5 (-3.0;12.5)	0.16	9.7 (3.1;16.7)	0.0078	3.0 (-2.7;9.0)	0.19	-0.9 (-6.2;4.7)	0.61	0.21	0.03
<b>6MWT (m)</b>	463.8 (80.0)	496.6 (92.1)	7.1 (8.6)	-2.4 (-6.2;1.5)	0.85	-2.4 (-6.6;2.0)	0.82	0.7 (-3.2;4.7)	0.38	2.6 (-0.73;6.1)	0.099	0.11	0.16
<b>9HPT (s)</b>	17.2 (3.9)	16.8 (3.4)	3.1 (11.3)	-4.6 (-10.3;1.5)	0.89	-0.2 (-5.3;5.2)	0.52	0.3 (-5.7;6.6)	0.47	1.2 (-3.4;6.0)	0.33	0.15	0.092
<b>Ankle Dorsiflexion (Nm)</b>	8.4 (5.7)	7.8 (4.7)	33.1 (223.2)	-4.0 (-21.7;17.8)	0.63	11.4 (-15.4;46.8)	0.26	8.2 (-13.8;35.9)	0.28	5.5 (-12.8;27.7)	0.32	0.11	0.16
<b>Grip (kg)</b>	22.4 (8.7)	23.5 (9.7)	5.1 (17.9)	-7.1 (-15.6;2.1)	0.9	-3.6 (-11.8;5.4)	0.75	1.6 (-7.7;11.9)	0.39	6.0 (-1.2;13.7)	0.088	0.12	0.15
<b>CMAP (milliV)</b>	3.8 (2.0)	4.0 (2.0)	19.6 (56.5)	-25.1 (-44.8;1.5)	0.94	-9.2 (-27.3;13.5)	0.77	-5.1 (-27.1;23.6)	0.63	6.6 (-15.8;35.1)	0.33	-0.0011	0.5
<b>MCV (m/s)</b>	21.6 (4.4)	22.2 (4.7)	4.2 (10.9)	-1.0 (-6.5;4.9)	0.61	0.5 (-4.8;6.2)	0.44	2.8 (-3.4;9.4)	0.23	2.5 (-2.4;7.7)	0.21	0.11	0.18
<b>DML (ms)</b>	8.2 (2.0)	7.9 (2.0)	6.7 (25.6)	3.4 (-4.3;11.7)	0.24	13.8 (4.2;24.3)	0.0092	8.0 (0.59;16.0)	0.038	2.2 (-5.1;10.0)	0.31	0.21	0.035
<b>SNAP (microV)</b>	2.5 (3.3)	2.8 (3.4)	15.9 (110.2)	-1.2 (-42.9;71.0)	0.52	8.7 (-31.2;71.6)	0.38	13.9 (-24.1;71.0)	0.29	12.0 (-23.9;64.9)	0.31	0.089	0.3
<b>SCV (m/s)</b>	30.6 (10.7)	32.0 (9.2)	12.7 (38.0)	1.5 (-5.8;9.4)	0.36	17.5 (-5.5;46.2)	0.11	26.6 (15.5;38.8)	0.00037	20.1 (2.4;40.8)	0.03	0.42	0.0098
<b>VAS: Pain</b>	83.9 (18.9)	78.6 (21.2)	-2.4 (34.4)	-17.4 (-30.7;-1.6)	0.96	6.7 (-7.2;22.6)	0.22	-13.6 (-29.0;5.3)	0.89	-10.3 (-23.2;4.8)	0.88	-0.057	0.69
<b>VAS: Fatigue</b>	67.5 (22.4)	61.2 (24.7)	1.0 (57.1)	-25.6 (-43.1;-2.7)	0.96	-10.5 (-28.8;12.6)	0.79	-17.0 (-34.4;5.0)	0.91	-2.5 (-20.3;19.3)	0.58	-0.094	0.8
<b>VAS: Global</b>	67.5 (24.0)	72.4 (19.2)	38.0 (129.0)	-8.1 (-21.0;6.9)	0.82	-11.4 (-33.5;18.0)	0.76	-10.5 (-24.5;6.1)	0.86	-2.6 (-19.4;17.7)	0.59	-0.21	0.97
<b>CGI: Global Improvement</b>	4.0 (0.0)	3.9 (0.4)	3.2 (11.5)	1.5 (-2.2;5.3)	0.25	9.8 (4.0;16.0)	0.0032	-1.2 (-4.4;2.2)	0.72	-4.8 (-8.7;-0.69)	0.97	0.051	0.33
<b>CGI: Illness Severity</b>	3.5 (0.8)	3.5 (1.0)	5.6 (44.7)	-1.4 (-15.6;15.2)	0.56	-8.1 (-18.9;4.1)	0.87	-8.3 (-17.5;1.9)	0.91	-6.1 (-16.0;5.0)	0.82	-0.15	0.91
<b>CGI: Therapeutic Effect</b>	4.0 (0.0)	3.9 (0.4)	5.5 (16.3)	-0.1 (-3.5;3.3)	0.53	9.0 (1.1;17.5)	0.03	-1.5 (-4.0;1.0)	0.84	-4.3 (-8.8;0.36)	0.94	0.042	0.35