Supplemental Online Content

Petersen EA, Stauss TG, Scowcroft JA, et al. Effect of high-frequency (10-kHz) spinal cord stimulation in patients with painful diabetic neuropathy: a randomized clinical trial. *JAMA Neurol*. Published online April 5, 2021. doi:10.1001/jamaneurol.2021.0538

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Primary end point sensitivity analysis results

Population	Description	CMM	10 kHz SCS+CMM	p-value
1	Per Protocol (PP)	5/94 (5.3%)	75/87 (86.2%)	< 0.0001
2	ITT Known Status 10 kHz SCS	5/94 (5.3%)	75/95 (78.9%)	< 0.0001
3	ITT Worst Case for 10 kHz SCS LTF	5/94 (5.3%)	75/98 (76.5%)	< 0.0001
4	ITT Worst Case All Missing 10 kHz SCS	5/94 (5.3%)	75/112 (67.0%)	< 0.0001
5	ITT Worst 10 kHz SCS/Best CMM Case	12/103 (11.7%)	75/113 (66.4%)	< 0.0001

eTable 1: Primary endpoint sensitivity analyses. Subjects who did not complete the neurological assessment at 3 months were excluded from primary endpoint analysis of populations 1-4 for CMM (n=2) and populations 1-3 for 10 kHz SCS+CMM (n=1); ITT: intention-to-treat, LTF: lost to follow-up.

eTable 2. Pain visual analogue scale scores for patients excluded from the per-protocol population

	Baseline	End of Trial		1 Month		3 Months		6 Months	
	VAS (cm)	VAS (cm)	% Relief	VAS (cm)	% Relief	VAS (cm)	% Relief	VAS (cm)	% Relief
CMM Subject 1	4.80	NA	NA	Not done	-	Not done	-	1.05	78.1
CMM Subject 2	8.15	NA	NA	9.30	-14.1	Not done	-	9.60	-17.8
10 kHz SCS Subject 1	5.55	0.00	100	0.15	97.3	Not done	-	0.85	84.7

eTable 2: Individual lower limb pain scores and percentage relief from baseline for the subjects excluded from PP population. VAS: visual analog scale.

eTable 3. Summary of study-related adverse events

	CMM n = 103	10 kHz SCS + CMM n = 113
Total study-related AEs, n (# of subjects, %)	None reported	18 (14, 12.4%)
Rated as Serious AEs	-	2 (2, 1.8%)
Study-related AEs by type		
Infection	-	3 (3, 2.7%)
Wound dehiscence	-	2 (2, 1.8%)
Impaired healing	-	1 (1, 0.9%)
Device extrusion	-	1 (1, 0.9%)
Incision site pain	-	1 (1, 0.9%)
IPG site discomfort	-	1 (1, 0.9%)
Lead migration	-	1 (1, 0.9%)
Contact dermatitis	-	1 (1, 0.9%)
Urticaria	-	1 (1, 0.9%)
Radiculopathy	-	1 (1, 0.9%)
Uncomfortable stimulation	-	1 (1, 0.9%)
Gastroesophageal reflux	-	1 (1, 0.9%)
Myalgia	-	1 (1, 0.9%)
Arthralgia	-	1 (1, 0.9%)
Hyporeflexia	-	1 (1, 0.9%)

eTable 3: Summary of study-related adverse events (AEs). IPG: implantable pulse generator.

eTable 4. Summary of secondary end point analyses

	CMM	10 kHz SCS + CMM	Between-Group p-value
Per Protocol Population	**n=96[1]**	**n=88[1]**	
1. Lower limb pain VAS ≤3 cm at 3 months, % (n/n)	5.2% (5/96)	78.4% (69/88)	< 0.001[2]
2. Subjects crossing over at 6 months, % (n/n)	81.7% (76/93)	0.0% (0/87)	< 0.001[2]
3. Lower limb pain relief ≥50% at 6 months, % (n/n)	5.4% (5/93)	85.1% (74/87)	< 0.001[2]
4. Remitters[3] at 6 months, % (n/n)	1.1% (1/95)	60.2% (53/88)	< 0.001[2]
5. Overall improvement in neurological assessment[4] at 3 months, % (n/n)	6.4% (6/94)	72.4% (63/87)	< 0.001[2]
6. Overall improvement in neurological assessment[4] at 6 months, % (n/n)	3.3% (3/92)	61.9% (52/84)	< 0.001[2]
7. Changes in health-related quality of life at 6 months			
EQ-5D-5L index, mean ± SD	-0.031 ± 0.127	0.130 ± 0.159	< 0.001[5]
EQ-5D-5L health VAS, mean ± SD	-1.7 ± 23.0	15.9 ± 21.6	< 0.001[5]
8. Percentage change in HbA1c at 6 months, mean ± SD	2.6% ± 15.4%	1.5% ± 14.9%	0.649[5]

[1] The n for each assessment may vary due to missing data
[2] By Fisher's Exact test, 2-sided
[3] Remission is defined as pain VAS score ≤3 cm for 6 consecutive months
[4] Overall improvement on neurological assessment defined as no deficit compared to baseline in any motor, sensory, or reflex outcomes and improvement in at least one outcome
[5] Student's t-test, 2-sided

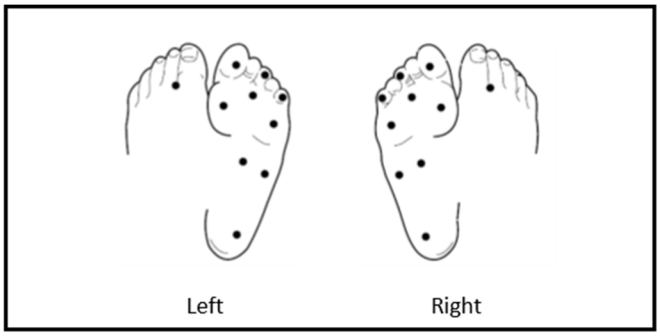
eTable 4: Summary of all prespecified secondary endpoints shown in order of hierarchical closed-testing procedure. There were statistically significant differences between the groups in the first 7 of 8 secondary endpoints. VAS: visual analog scale, cm: centimeter.

eTable 5. Pain visual analogue scale scores for patients who failed temporary trial spinal cord stimulation

	Baseline	End of Trial		1 Month CMM		3 Months CMM		6 Months CMM	
	VAS (cm)	VAS (cm)	% Relief	VAS (cm)	% Relief	VAS (cm)	% Relief	VAS (cm)	% Relief
Subject 1	6.75	6.10	9.6	3.75	44.4	Not done	-	Not done	-
Subject 2	9.30	4.95	46.8	4.15	55.4	3.40	63.4	6.25	32.8
Subject 3	6.65	4.85	27.1	Not done	-	3.95	40.6	5.30	20.3
Subject 4	7.30	5.20	28.9	8.55	-17.1	5.85	19.9	6.45	11.6
Subject 5	8.05	7.75	3.7	Not done	-	Not done	-	Not done	-
Subject 6	9.65	8.45	12.4	8.15	15.5	8.65	10.4	8.70	9.8

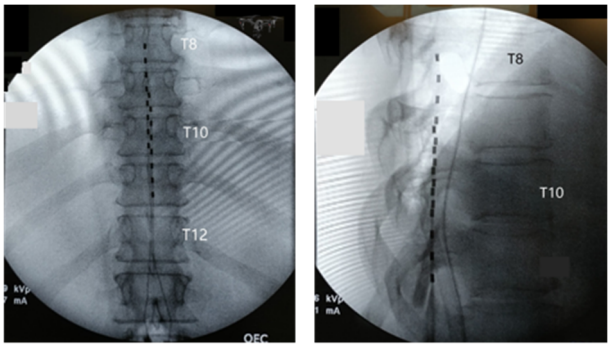
eTable 5: Individual lower limb pain scores and percentage relief from baseline for the trial failure subjects treated with CMM. VAS: visual analog scale.

eFigure 1. Diabetic foot examination



eFigure 1: Standardized test sites on the feet for 10-g monofilament & pinprick sensory examination. Outcome options for each test site include: hypersensitive, normal, diminished, or absent.

eFigure 2. Spinal cord stimulation lead placement



eFigure 2: Typical placement of stimulation electrodes along midline T8-T11 vertebral levels shown in anterior-posterior (left) and lateral (right) x-rays.