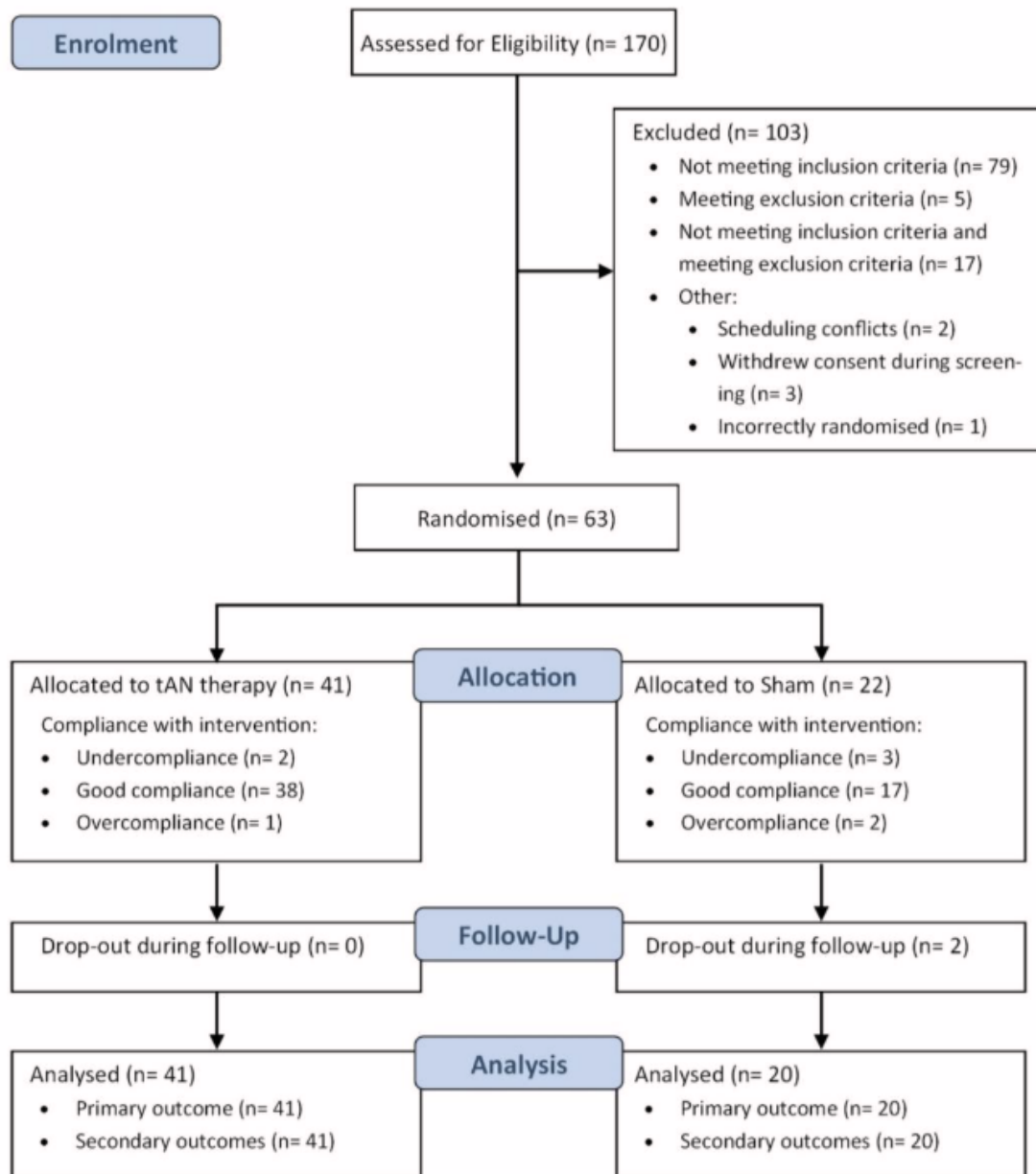


Participant Flow



Baseline Characteristics

1. Basic Characteristics.

Baseline characteristics	Whole cohort (N = 63)	tAN treatment (N = 41)	Sham (N = 22)
Age, y	47.2 (12.6)	49.2 (13.0)	43.5 (11.1)
Sex			
Male	45 (71.4)	30 (73.2)	15 (68.2)
Female	18 (28.6)	11 (26.8)	7 (31.8)
Ethnicity			
White	34 (54.0)	28 (68.3)	6 (27.3)
Mixed	4 (6.3)	2 (4.9)	2 (9.1)
Black	14 (22.2)	6 (14.6)	8 (36.4)
South Asian	8 (12.7)	4 (9.8)	4 (18.2)
Southeast Asian	3 (4.8)	1 (2.4)	2 (9.1)
BMI	31.4 (4.7)	30.9 (4.9)	32.3 (4.5)
Hypertension Duration in years (Median (IQR))	5 (2-10.5)	4 (2-9)	7 (5-14)
Missing	3	0	3
Number of comorbidities (Median (IQR))	2 (1-4)	2 (1-5)	2 (1-3)
Missing	1	1	0
Type of comorbidity			
Diabetes	3 (4.8)	2 (5.0)	1 (4.5)
Obstructive Sleep Apnoea	6 (9.7)	3 (7.5)	3 (13.6)
Hyperlipidaemia	10 (16.1)	4 (10.0)	6 (27.3)
Hypercholesterolemia	7 (11.3)	3 (7.5)	4 (18.2)
Number of anti-hypertensives (Median (IQR))	2 (1-2)	1 (1-2)	2 (1-2)
Medication class			
ACE inhibitors	11 (17.5)	8 (19.5)	3 (13.6)
Angiotensin II receptor blocker	28 (44.4)	16 (39.0)	12 (54.5)
Beta blockers	2 (3.2)	1 (2.4)	1 (4.5)
Calcium channel blocker	38 (60.3)	24 (58.5)	14 (63.6)
Diuretics	16 (25.4)	9 (22.0)	7 (31.8)
Others	7 (11.1)	5 (12.2)	2 (9.1)
Measures at screening			
HbA1c	36.2 (6.8)	36.2 (7.4)	36.4 (5.7)
LDL	2.7 (0.9)	2.7 (0.8)	2.8 (1.0)
Total cholesterol	4.9 (0.9)	4.9 (0.9)	4.9 (1.1)
Creatinine	85.5 (15.3)	83.3 (12.9)	89.5 (18.6)
eGFR	77.6 (11.4)	78.8 (11.6)	75.5 (10.7)
BP, mmHg			

Baseline Characteristics

1. Basic Characteristics.

Baseline characteristics	Whole cohort (N = 63)	tAN treatment (N = 41)	Sham (N = 22)
Daytime ambulatory SBP	149.8 (9.9)	149.9 (10.0)	149.7 (9.8)
Daytime ambulatory DBP	95.1 (6.9)	95.0 (7.2)	95.4 (6.5)
Office SBP	148.5 (14.6)	148.0 (14.4)	149.4 (15.2)
Office DBP	94.6 (9.8)	93.6 (8.7)	96.3 (11.5)
24-hour ambulatory SBP	146.4 (9.8)	146.0 (10.1)	147.3 (9.5)
24-hour ambulatory DBP	92.1 (6.8)	91.8 (7.1)	92.9 (6.3)
SBP variability (coefficient of variation (IQR))	10.0 (8.5-11.9)	10.3 (9.2-12.5)	9.2 (7.3-10.8)
HR, beats/min			
Daytime ambulatory HR	80.3 (8.7)	81.0 (8.6)	79.1 (9.0)
Nighttime ambulatory HR	72.4 (10.0)	71.9 (9.9)	73.5 (10.3)
ISI (median (IQR))	9 (4-14)	12 (6-14)	7 (4-10)
EQ5D (Index score)	0.92 (0.86-1.00)	0.92 (0.86-1.00)	0.93 (0.86-1.00)
6MWT, metres	414.4 (61.6)	412.3 (67.8)	418.2 (49.0)
<i>Note.</i> Values are mean (SD) or n (%) if not otherwise stated. BMI = body mass index; BP = blood pressure; SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate; ISI = insomnia severity index; EQ5D = EuroQol 5-Dimension Questionnaire; 6MWT = Six-Minute Walk Test.			

Outcome Measures

2. Primary outcome. Crude and adjusted linear regression models relating the change in daytime SBP from baseline to the end of treatment (3 months) to treatment allocation (tAN vs. sham).

<i>Predictor</i>	Unadjusted crude difference		Adjusted difference ¹	
	Difference (95% CI)	P-value	Difference (95% CI)	P-value
Treatment arm (tAN treatment vs. Sham)	2.35 (-4.37, 9.07)	0.486	2.86 (-3.79, 9.51)	0.392
Adjusted analysis variables				
Baseline SBP	n/a	n/a	-0.33 (-0.65, -0.01)	0.041*
Age	n/a	n/a	-0.10 (-0.17, 0.38)	0.456
Sex (Female vs. Male)	n/a	n/a	4.27 (-2.70, 11.24)	0.225
BMI	n/a	n/a	0.62 (-0.08, 1.32)	0.080
<i>Note.</i> *significance at the $p < 0.05$ level. SBP = systolic blood pressure. BMI = body mass index.				

3. Secondary outcomes. Change in daytime, 24hr ABPM, and office SBP and DBP at 1 month and 3 months vs. baseline in tAN treatment and sham (N = 61).

Outcome	1 month change vs. baseline (95% CI) ¹				3 months change vs baseline (95% CI) ¹			
	tAN treatment (n = 41)	Sham (n = 20)	Between-group mean diff (95% CI)	<i>p</i>	tAN treatment (n = 41)	Sham (n = 20)	Between-group mean diff (95% CI)	<i>p</i>
Daytime ABPM SBP	-1.56 (-4.96, 1.84)	-0.55 (-5.55, 4.45)	-1.01 (-6.87, 4.85)	0.73	-3.15 (-7.17, 0.88)	-5.5 (-10.79, -0.21)	2.35 (-4.37, 9.07)	0.49
Daytime ABPM DBP	-1.32 (-3.73, 1.10)	0.15 (-3.91, 4.21)	-1.47 (-5.83, 2.90)	0.50	-2.59 (-5.46, 0.29)	-3.35 (-6.60, -0.10)	0.76 (-3.86, 5.39)	0.74
24hr ABPM SBP	-2.39 (-6.06, 1.28)	-0.75 (-5.72, 4.22)	-1.64 (-7.81, 4.53)	0.60	-2.98 (-6.96, 1.01)	-5.05 (-10.36, 0.26)	2.07 (-4.60, 8.74)	0.54
24hr ABPM DBP	-1.39 (-3.65, 0.87)	0.35 (-3.79, 4.49)	-1.74 (-5.97, 2.49)	0.41	-2.46 (-5.19, 0.26)	-3.00 (-6.20, 0.20)	0.54 (-3.88, 4.96)	0.81
Office SBP	-0.39 (-5.10, 4.31)	-0.15 (-9.33, 9.03)	-0.24 (-9.29, 8.80)	0.96	-1.68 (-7.34, 3.98)	-4.80 (-11.81, 2.21)	3.12 (-6.18, 12.41)	0.51
Office DBP	-1.73 (-4.25, 0.80)	1.05 (-4.93, 7.03)	-2.78 (-8.12, 2.57)	0.30	-2.10 (-5.74, 1.55)	-2.20 (-7.07, 2.67)	0.10 (-6.01, 6.21)	0.97

Note. ¹Change in parameters over 1 month are calculated by subtracting the baseline recording from the 1-month recording. Change in parameters over 3 months is calculated by subtracting the baseline recording from the 3-month recording. Between-group mean difference is calculated by subtracting the change in sham from the change in tAN. All values recorded in mmHg (95% CI). P-values comes from two sample t-tests with equal variance. ABPM = ambulatory blood pressure monitor; SBP = systolic blood pressure; DBP = diastolic blood pressure.

4. Secondary outcomes. Change in daytime and nighttime ambulatory heart rate, and SBP variability at 3 months vs. baseline in tAN treatment and sham (N = 61).

Outcome	3 months change vs baseline ³			
	tAN treatment (n = 41)	Sham (n = 20)	Between-group diff (95% CI)	p
Daytime ambulatory heart rate ¹	0.56 (-1.71, 2.83)	0.55 (-2.34, 3.44)	0.01 (-3.75, 3.77)	1.00
Nighttime ambulatory heart rate ¹	0.27 (-2.58, 3.12)	-0.85 (-5.26, 3.56)	1.12 (-3.88, 6.12)	0.66
24hr ABPM SBP variability ²	-0.18 (-1.91, 2.07)	-0.01 (-1.86, 1.50)	0.03 (-1.32, 1.41)	0.98
Office SBP variability ²	-0.29 (-1.6, 1.35)	0.71 (-1.30, 1.77)	-0.66 (-2.02, 0.85)	0.36
<i>Note.</i> ¹Mean (95% CI). P values comparing difference in the change in mean scores are derived from two sample t-test with equal variance. Heart rate data are derived from ABPM. ²Median (interquartile range). Hodges-Lehmann median difference between study arms with 95% Confidence Interval. P-values derived from Mann Whitney U test. SBP variability reported as coefficient of variation. ³For each outcome, the change over 3 months is calculated by subtracting the baseline recording from the 3-month recording. Between-group mean difference is calculated by subtracting the change in sham from the change in tAN.				

5. Secondary outcomes. Change in Holter indices of heart rate variability from baseline to 1 month and 3 months in tAN and sham (N=61).

Outcome	1 month change vs. baseline				3 months change vs. baseline			
	tAN treatment (n = 41) ¹	Sham (n = 20) ¹	Between-group mean diff (95% CI) ²	p	tAN treatment (n = 41) ¹	Sham (n = 20) ¹	Between-group mean diff (95% CI) ²	p
HR mean	0.73 (5.91)	-0.58 (5.67)	1.31 (-1.99, 4.61)	0.43	1.67 (5.67)	-0.89 (4.79)	2.56 (-0.47, 5.59)	0.10
QTc Average	4.70 (124.45)	31.36 (121.11)	-26.66 (-96.12, 42.81)	0.45	8.16 (66.27)	-1.25 (166.14)	5.08 (-23.32, 33.47)	0.76
QTc SD	-2.5 (21.48)	6.3 (25.72)	-8.8 (-21.72, 4.12)	0.18	-0.76 (1.29)	3.17 (2.96)	0.53 (-5.40, 6.46)	0.54
SDNN	-19.74 (66.88)	14.47 (52.26)	-34.21 (-69.39, 0.97)	0.06	-8.23 (53.65)	0.79 (85.98)	-9.02 (-45.90, 27.86)	0.63
SDNNi	-4.55 (27.65)	10.58 (35.44)	0.49 (-7.73, 8.72)	0.08	-1.92 (10.69)	3.37 (54.77)	-0.19 (-8.63, 8.25)	0.56
RMSDD	-1.5 (20.91)	9.47 (32.81)	-10.97 (-25.29, 3.34)	0.13	-0.744 (6.89)	2.95 (44.85)	-3.69 (-18.29, 10.91)	0.62
sNN50	376.13 (3266.51)	1228.32 (3533.47)	-852.18 (-2742.03, 1037.66)	0.37	-352 (2083.26)	841.21 (3722.73)	-1193.21 (-2717.76, 331.34)	0.12
TRIINDEX	-5.13 (24.93)	3.95 (30.36)	-9.08 (-24.19, 6.03)	0.23	-1.59 (10.13)	-0.74 (44.54)	-0.85 (-15.76, 14.05)	0.91
QT Average	-15.92 (77.81)	24.46 (101.55)	-40.39 (-88.98, 8.21)	0.10	-3.50 (24.20)	2.7 (148.30)	-6.20 (-54.62, 42.23)	0.80
Note. ¹Mean (SD). ²Mean difference between treatment arms with 95% confidence interval.								

For each outcome, the change in Holter parameter over 1 month is calculated by subtracting the baseline Holter parameter from the 1-month Holter parameter. The change over 3 months is calculated by subtracting the baseline Holter parameter from the 3-month Holter parameter. Between-group mean difference is calculated by subtracting the change in sham from the change in tAN.

HR = heart rate, SD = standard deviation, SDNN = standard deviation of normal-to-normal intervals, RMSDD = root mean square of successive differences, sNN50 = successive normal-to-normal intervals exceeding 50 milliseconds, TRIINDEX = triangular index.

6. Secondary outcomes. Change in Insomnia Severity Index, EQ-5D Index, EQ-5D visual analogue, and 6MWT score at 1 month and 3 months vs. baseline in tAN treatment and sham (N = 61).

Outcome	1 month change vs. baseline				3 months change vs. baseline			
	tAN treatment (n = 41)	Sham (n = 20)	Between-group diff (95% CI)	p	tAN treatment (n = 41)	Sham (n = 20)	Between-group diff (95% CI)	p
ISI ¹	-1 (-2-2)	0 (-2-1.5)	0 (-1,1)	0.97	-1 (-4-2)	-0.5 (-3-1)	0 (-2, 2)	0.88
EQ-5D Index ¹	0.00 (0.00-0.05)	0.00 (0.00-0.06)	0.00 (-0.03, 0.02)	0.94	0.00 (-0.02-0.05)	0.00 (0.00-0.03)	0.00 (-0.03, 0.01)	0.78
EQ-5D visual analogue ¹	0 (-10- 10)	0 (-7.5-5)	0 (-5, 7)	0.88	0 (-5, 10)	0 (-5 -10)	0 (-5, 7)	0.78
6MWT ²	23.6 (7.4, 40.0)	16.7 (-5.2, 38.6)	7.0 (-20.4, 34.3)	0.61	27.5 (9.6, 45.3)	17.6 (10.8, 38.0)	9.9 (-19.4, 39.3)	0.50
<i>Note.</i> ¹Median (interquartile range). ²Mean (95% CI). P values comparing difference in the change in mean scores are derived from two sample t-test with equal variance. P values comparing difference in the change in median scores are derived from Mann-Whitney U test and between group difference for change in median scores come from Hodges-Lehmann median difference between treatments arms with 95% confidence interval. ISI = Insomnia Severity Index; EQ-5D = EuroQol 5-Dimension; 6MWT = 6-Minute Walk Test.								

7. Secondary outcomes. Difference in device adherence between treatment arms.

	tAN treatment (N = 41)	Sham (N = 20)	Difference in proportions (95% CI)²	P-value³
Proportion of the number of days when treatment was self-administered ¹	100 (95.8–100)	100 (100–100)	0 (-4.2, 0)	0.60
Average Daily Duration (minutes) over 3 months of treatment ¹	30 (30–30)	30 (30–30)	0 (0, 0)	0.56
<i>Note.</i> ¹ Median (interquartile range). ² Hodges-Lehmann median difference between study arms with 95% Confidence Interval. ³ P-values derived from Mann Whitney U test.				

Harms/Adverse Events

8. Adverse events not related to devices grouped by system organ class and severity for each trial arm (N=63).

	tAN treatment (N = 41)			Sham (N = 22)		
	Mild	Moderate	Overall	Mild	Moderate	Overall
	51	35	86	16	16	32
Total						
Cardiac Disorders	5 (5.8)	7 (8.1)	12 (14.0)	3 (9.4)	2 (6.3)	5 (15.6)
Abnormal blood pressure	0 (0)	1 (1.2)	1 (1.2)	0 (0)	1 (3.1)	1 (3.1)
Cardiomyopathy	–	–	–	1 (3.1)	0 (0)	1 (3.1)
Echo abnormality	0 (0)	3 (3.5)	3 (3.5)	1 (3.1)	0 (0)	1 (3.1)
Hypertensive heart disease	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Lightheadness	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Left ventricular diastolic dysfunction	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Left ventricular hypertrophy	0 (0)	2 (2.3)	2 (2.3)	1 (3.1)	1 (3.1)	2 (6.3)
Tachycardia	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Tricuspid regurgitation	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Ventricular tachycardia	0 (0)	1 (1.2)	1 (1.2)	–	–	–
Congenital, familial and genetic disorders	–	–	–	0 (0)	1 (3.1)	1 (3.1)
Bicuspid aortic valve	–	–	–	0 (0)	1 (3.1)	1 (3.1)
Ear and Labyrinth disorders	3 (3.5)	1 (1.2)	4 (4.7)	0 (0)	2 (6.3)	2 (6.3)
Earache	1 (1.2)	1 (1.2)	2 (2.3)	–	–	–
Ear infection	2 (2.3)	0 (0)	2 (2.3)	0 (0)	1 (3.1)	1 (3.1)
Tinnitus	–	–	–	0 (0)	1 (3.1)	1 (3.1)
Endocrine disorders	2 (2.3)	0 (0)	2 (2.3)	–	–	–
Non-insulin dependent diabetes	2 (2.3)	0 (0)	2 (2.3)	–	–	–
Eye disorders	–	–	–	1 (3.1)	0 (0)	1 (3.1)
Blurry vision	–	–	–	1 (3.1)	0 (0)	1 (3.1)
Gastrointestinal disorders	2 (2.3)	7 (8.1)	9 (10.5)	1 (3.1)	0 (0)	1 (3.1)
Barrett's oesophagus	0 (0)	1 (1.2)	1 (1.2)	–	–	–

Bloating	0 (0)	1 (1.2)	1 (1.2)	–	–	–
Diverticulitis aggravated	0 (0)	1 (1.2)	1 (1.2)	–	–	–
Dry mouth	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Gastritis	0 (0)	1 (1.2)	1 (1.2)	–	–	–
Hiatus Hernia	0 (0)	1 (1.2)	1 (1.2)	–	–	–
Stomach pain	0 (0)	1 (1.2)	1 (1.2)	–	–	–
Stomach upset	0 (0)	1 (1.2)	1 (1.2)	1 (3.1)	0 (0)	1 (3.1)
Toothache	1 (1.2)	0 (0)	1 (1.2)	–	–	–
General disorders and administration site conditions	5 (5.8)	2 (2.3)	7 (8.1)	2 (6.3)	1 (3.1)	3 (9.4)
Dizziness	3 (3.5)	0 (0)	3 (3.5)	0 (0)	1 (3.1)	1 (3.1)
Fatigue	1 (1.2)	1 (1.2)	2 (2.3)	1 (3.1)	0 (0)	1 (3.1)
General body pain	0 (0)	1 (1.2)	1 (1.2)	–	–	–
Mood swings	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Skin rash	–	–	–	1 (3.1)	0 (0)	1 (3.1)
Infections and Infestations	3 (3.5)	0 (0)	3 (3.5)	–	–	–
Foot infection	2 (2.3)	0 (0)	2 (2.3)	–	–	–
Leg infection	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Injury, poisoning and procedural complications	4 (4.7)	1 (1.2)	5 (5.8)	3 (9.4)	1 (3.1)	4 (12.5)
Abrasion	–	–	–	1 (3.1)	0 (0)	1 (3.1)
Administration site bruise	1 (1.2)	0 (0)	1 (1.2)	0 (0)	1 (3.1)	1 (3.1)
Fall	1 (1.2)	1 (1.2)	2 (2.3)	–	–	–
Procedural headache	–	–	–	1 (3.1)	0 (0)	1 (3.1)
Shoulder pain	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Vessel puncture site pain	1 (1.2)	0 (0)	1 (1.2)	1 (3.1)	0 (0)	1 (3.1)
Metabolism and nutrition disorders	2 (2.3)	1 (1.2)	3 (3.5)	–	–	–
Hypertriglyceridemia	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Hypokalaemia	1 (1.2)	1 (1.2)	2 (2.3)	–	–	–
Musculoskeletal and connective tissue disorders	5 (5.8)	3 (3.5)	8 (9.3)	0 (0)	5 (15.6)	5 (15.6)

Back pain	1 (1.2)	0 (0)	1 (1.2)	0 (0)	2 (6.3)	2 (6.3)
Chest pain	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Foot pain	–	–	–	0 (0)	1 (3.1)	1 (3.1)
Jaw pain	0 (0)	1 (1.2)	1 (1.2)	–	–	–
Knee pain	1 (1.2)	2 (2.3)	3 (3.5)	0 (0)	1 (3.1)	1 (3.1)
Leg cramps	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Muscle pain	–	–	–	0 (0)	1 (3.1)	1 (3.1)
Neck pain	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Nervous system disorders	5 (5.8)	5 (5.8)	10 (11.6)	2 (6.3)	1 (3.1)	3 (9.4)
Chronic paroxysmal hemicrania	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Headache	4 (4.7)	1 (1.2)	5 (5.8)	1 (3.1)	1 (3.1)	2 (6.3)
Migraine	0 (0)	4 (4.7)	4 (4.7)	1 (3.1)	0 (0)	1 (3.1)
Psychiatric disorders	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Panic attack	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Renal and Urinary disorders	4 (4.7)	2 (2.3)	6 (7.0)	0 (0)	1 (3.1)	1 (3.1)
Kidney pain	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Proteinuria	–	–	–	0 (0)	1 (3.1)	1 (3.1)
Pyelonephritis	0 (0)	1 (1.2)	1 (1.2)	–	–	–
Renal impairment	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Urine incontinence	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Urinary Tract Infection	1 (1.2)	1 (1.2)	2 (2.3)	–	–	–
Respiratory, thoracic and mediastinal disorders	6 (7.0)	6 (7.0)	12 (14.0)	4 (12.5)	2 (6.3)	6 (18.8)
Chest infection	1 (1.2)	1 (1.2)	2 (2.3)	–	–	–
Cough	2 (2.3)	1 (1.2)	3 (3.5)	–	–	–
COVID infection	0 (0)	1 (1.2)	1 (1.2)	0 (0)	1 (3.1)	1 (3.1)
Head cold	1 (1.2)	2 (2.3)	3 (3.5)	1 (3.1)	0 (0)	1 (3.1)
Influenza	1 (1.2)	0 (0)	1 (1.2)	1 (3.1)	1 (3.1)	2 (6.3)
Pneumonia	0 (0)	1 (1.2)	1 (1.2)	–	–	–
Sinusitis	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Sore throat	–	–	–	1 (3.1)	0 (0)	1 (3.1)

Upper respiratory tract infection	–	–	–	1 (3.1)	0 (0)	1 (3.1)
Skin and subcutaneous disorders	4 (4.7)	0 (0)	4 (4.7)	–	–	–
Dermatitis	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Dysplastic naevus	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Paraesthesia	1 (1.2)	0 (0)	1 (1.2)	–	–	–
Skin irritation	1 (1.2)	0 (0)	1 (1.2)	–	–	–
<i>Note.</i> Numbers are presented with % of total adverse events in each trial arm (tAN treatment: n=86, Sham: n=32).						

9. Adverse Device Effects grouped by System Organ Class and severity for each trial aim (N=63).

Adverse Device Effects	tAN therapy (N = 41)			Sham (N = 22)		
	Mild	Moderate	Overall	Mild	Moderate	Overall
Total	23	3	26	5	0	5
Cardiac Disorders	3 (11.5%)	0 (0%)	3 (11.5%)	1 (20.0%)	0	1 (20.0%)
Arrhythmia	1 (3.9%)	0 (0%)	1 (3.9%)	–	–	–
Lightheadness	1 (3.9%)	0 (0%)	1 (3.9%)	1 (20.0%)	0 (0%)	1 (20.0%)
Palpitations	1 (3.9%)	0 (0%)	1 (3.9%)	–	–	–
General disorders and administration site conditions	13 (50.0%)	0 (0%)	13 (50.0%)	4 (80.0%)	0 (0%)	4 (80.0%)
Burning sensation in face	1 (3.9%)	0 (0%)	1 (3.9%)	–	–	–
Ear pain	6 (23.1%)	0 (0%)	6 (23.1%)	2 (40.0%)	0 (0%)	2 (40.0%)
Fuzzy head	1 (3.9%)	0 (0%)	1 (3.9%)	–	–	–
Skin irritation	1 (3.9%)	0 (0%)	1 (3.9%)	–	–	–
Tingling	4 (15.4%)	0 (0%)	4 (15.4%)	2 (40.0%)	0 (0%)	2 (40.0%)
Musculoskeletal and connective tissue disorders	1 (3.9%)	0 (0%)	1 (3.9%)	–	–	–
Jaw pain	1 (3.9%)	0 (0%)	1 (3.9%)	–	–	–
Nervous system disorders	2 (7.7%)	2 (7.7%)	4 (15.4%)	–	–	–
Headache	0 (0%)	1 (3.9%)	1 (3.9%)	–	–	–
Head discomfort	1 (3.9%)	0 (0%)	1 (3.9%)	–	–	–
Head pain	1 (3.9%)	0 (0%)	1 (3.9%)	–	–	–
Loss of consciousness	0 (0%)	1 (3.9%)	1 (3.9%)	–	–	–
Psychiatric disorders	0 (0%)	1 (3.9%)	1 (3.9%)	–	–	–
Altered mood	0 (0%)	1 (3.9%)	1 (3.9%)	–	–	–

Skin and subcutaneous disorders	4 (15.4%)	0 (0%)	4 (15.4%)	—	—	—
Burning sensation	2 (7.7%)	0 (0%)	2 (7.7%)	—	—	—
Skin irritation	2 (7.7%)	0 (0%)	2 (7.7%)	—	—	—

