Supplementary material

Stec S, Jankowska-Polańska B, et al. Rationale and Design of SAN.OK Randomized Clinical Trial and Registry: Comparison of the Effects of Evidence-Based Pacemaker Therapy And Cardioneuroablation in Sinus Node Dysfunction

Table S1. Study sites of SAN.OK Trial and Registry.

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Table S2. Schedule of enrolment, interventions, and assessments of SAN.OK Study and Registry in group A and CA (protocol version 05).

TIMEPOINT	V 0	V 1	V 2	V 3	V 4	V 5	V 6	V 7
	OUTPTATIENT	HOSPITAL		OUTATIENT				
	Screening	H1	H2	1 Month	3 Month	6 Month	9 Month	12 Month
Eligibility screen	X							
Informed consent	X							
Pregnancy test	X*	X*		X*	X*	X*	X*	X*
History and physical examination	X	X		X	X	X	X	X
Echocardiography (TTE)	X		X		X	X		X
24 hour Holter ECG	X		X		X	X		X
Holter ABPM	X		X		X	X		X
Exercise Tolerance Test	X		X		X	X		X
Autonomic tests (Valsalva, carotid massage, FBT, HUT, atropine challenge)	X					X		X
Randomization		X[1]						
PM implantation		X						
PM interrogation			X	X	X	X	X	X
Questionnaires (bradycardia, QOL, fatigue, depression/ anxiety, sleep)	X				X	X		X
Interdisciplinary consultations		X						
Review of adverse events		X	X	X	X	X	X	X

[1] Only group A

* Test carried out on patients in childbearing age

** VAS - Visual Analog Scale, QOL - quality of life, MFIS - Modified Fatigue Impact Scale, HADS-M - Modified Hospital Anxiety and Depression Scale, ESS - Epworth Sleep Scale, AIS-8 - Athens Insomnia Scale-8

Abbreviations: TEE- Transthoracic Echocardiography, ABPM – Ambulatory Blood Pressure Monitoring, FBT – Forced Breathing Test, HUT – Head-Up Tilt, HI-1- admission to the hospital, HI-2- discharge form hospital

Table S3. Schedule of enrolment, interventions, and assessments of SAN.OK Study and Registry in group B and CB (protocol version 05).

TIME POINT	V 0	V 1	V 2	V 3	V 4	V 5	V 6	V 7
	OUTPATIENT	HOSP I		HOSP II	OUTPATIENT			
	Screening	HI-1	HI-2	1 Month	3 Month	6 Month	9 Month	12 Month
Eligibility screen	X							
Informed consent	X							
Pregnancy test	X*	X*		X*	X*	X*	X*	X*
History (bradycardia symptoms) and physical examination	X	X		X	X	X	X	X
Echocardiography (TTE)	X		X	X	X	X	X	X
Holter ABPM	X		X	X	X	X		X
Exercise Tolerance Test	X				X	X		X
Autonomic tests (Valsalva, carotid massage, FBT, HUT, atropine challenge)	X					X		X
Randomization		X[1]						
ILR implantation and remote monitoring		X	X	X	X	X	X	X
EPS				X				
CNA				X				
ECVNS				X				
Questionnaires: bradycardia - VAS, QOL, fatigue (MFIS) depression/anxiety (HADS-M), sleep (ESS, AIS-8)	X				X	X		X
Interdisciplinary consultations		X						
Reassessment of indications for PM implantation					X	X	X	X
Review of adverse events				X	X	X	X	X

[1] Only group B

* Test carried out on patients in childbearing age

** VAS - Visual Analog Scale, QOL - quality of life, MFIS - Modified Fatigue Impact Scale, HADS-M - Modified Hospital Anxiety and Depression Scale, ESS - Epworth Sleep Scale, AIS-8 - Athens Insomnia Scale-8

Abbreviations: TEE- Transthoracic Echocardiography, ABPM – Ambulatory Blood Pressure Monitoring, FBT – Forced Breathing Test, HUT – Head-Up Tilt

Table S4. Secondary endpoints of SAN.OK Trial and Registry.

- Occurrence of major adverse cardiac events (peri-procedural and long-term complications): death, stroke, myocardial infarction, pericardial effusion requiring drainage, AV block, venous thrombosis, infection, hemorrhage, hematoma, fistula, pseudoaneurysm, surgical intervention
- Frequency of post-ablation inducibility of sinus arrest and/or AV block in pre- and post-procedural extracardiac vagal nerve stimulation (ECVNS)
- Assessment of long-term efficacy and safety of the treatment strategy
- Assessment of the effect of CNA on bradycardia symptoms, QOL, fatigue, depression /anxiety and sleep disorders based on standardized questionnaires at 0, 3, 6, 12 months
- Assessment of the non-invasive autonomic tests before and after the procedure in the period of 12 months
- Assessment of the frequency of bruxism and its resolution after treatment of bradycardia at 0, 6 and 12 months
- Assessment of incidence of sleep apnea and its resolution after treatment of bradycardia at 0, 6, 12 months
- Assessment of the decision to choose the treatment strategy