Synopsis

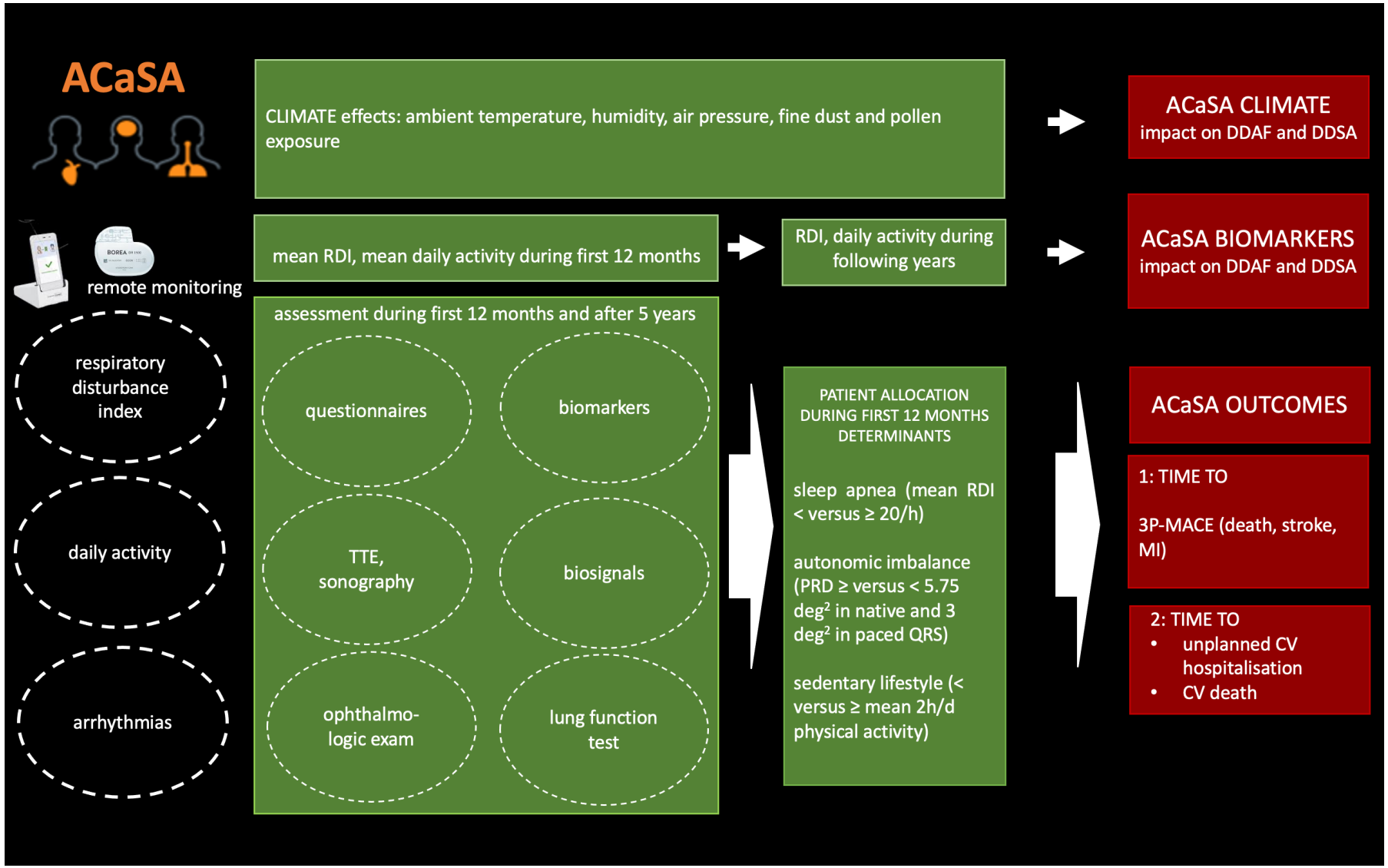
Title	Pacemaker-based long-term monitoring of sleep apnea
Medical Device	Microport TEO® SR/DR, Microport BOREA® SR/DR, Microport ALIZEA® SR/DR
Indication	Pacemaker implantation according to current ESC guidelines
Study design	prospective non-interventional cohort study
Location	multicenter
Duration of the clinical trial / schedule	Recruitment time: 10 years Planned first patient first visit (FPFV): November 2021 Planned last patient last visit (LPLV): December 2041 Treatment duration 5 - 20 years
Discriminators	• severe sleep apnea, defined by an average RDI ≥20/h measured by pacemaker system in the first year after study inclusion (= observation phase). • autonomic cardiac dysfunction defined by a PRD ≥ 5.75 deg^2 (nativ) or ≥ 3 deg^2 (paced) measured by 20-minute risk ECG in the first year after study inclusion (= observation phase). • physical inactivity, defined by an average of < 2 hours of daily exercise measured by pacemaker system in the first year after study inclusion (= observation phase).
Primary objective	• Time to first occurrence of 3P-MACE (spontaneous myocardial infarction, stroke or death), follow up for 120 months • Time to first device-detected atrial fibrillation (first epidoe lasting more than 6 minutes or 24 hours(, follow up for 120 months • Total burden of device-detected atrial fibrillation after 1, 3, 5 years • Incidence of severe device-detected sleep apnea (RDI ≥ 20/h) after 1, 3, 5 years • Variability of device-detected sleep apnea after 1, 3, 5 years
Secondary objectives	• Incidence of common opthalmological diseases in correlation to device-detected sleep apnea and device-detected atrial fibrillation, assessed within the first year after study enrolment • Deterioration of lung function conventional lung function testing after 5 years • Progression of subclinical peripheral artery disease, assessed by sonography, after 5 years • Progression of subclinical peripheral artery disease, assessed by ABI, after 5 years

	• QoL assessment by EQ-5D-5L questionnaires, after 5 years (compared to baseline)
Sample size	1000
Inclusion criteria / Exclusion criteria	**Inclusion criteria**: • Patients with an implanted Microport TEO® SR/DR, BOREA® SR/DR, ALIZEA® SR/DR pacemaker and a fully functional system • Signed informed consent from the patient **Exclusion criteria**: • end-stage kidney disease (eGFR < 15 ml/min/1.73 m^2) or renal-replacement therapy • Addiction or another disease that does not allow the patient to assess the nature and scope as well as possible consequences of the clinical trial. • Indications that the patient is unlikely to comply with the protocol (e.g., unwillingness to cooperate, inability to complete follow-up examinations). • Women of childbearing age • Women in pregnancy or lactation period • Life expectancy < 1 year
Study timeline	Visit 1: Inclusion and obtaining written / verbal consent. Pacemaker follow-up. Start of telemedical monitoring of the pacemaker system using SMARTVIEW® technology. Visit 2: Pacemaker follow-up within the first year. Performance and discussion of the examinations (20 min risk ECG, laboratory tests, TTE, questionnaires ESS & STOP Bang & EQ-5D-5L; optional spirometry, ABPM, sonography of the peripheral vessels with ABI measurement, ophthalmologic examinations). Visit 3: Pacemaker follow-up after 5 to 7 years. Discussion and optimization of telemedical monitoring of the pacemaker system using SMARTVIEW® technology. Performance and discussion of examinations (20 min risk ECG, laboratory tests, TTE, questionnaires ESS & STOP Bang & EQ-5D-5L; optional spirometry, ABPM, sonography of peripheral vessels with ABI measurement, ophthalmologic examinations). End of study: The end will occur at the scheduled end of study in December 2041.
Statistical methods and analysis	Kaplan-Meier curves are generated with respect to the primary combined and secondary endpoints and analysed with Cox proportional hazards models. Univariable and multivariable regression models are used to analyse multifactorial risk stratification, as are ROC analyses.

Study timeline

√ * optional; √ § The following laboratory values must be measured: hs-TnT, NT-proBNP, ferritin, transferrin saturation, hemoglobin, GGT, sodium, potassium, creatinine, urea, eGFR, CRP, leukocytes, platelets, total cholesterol, LDL cholesterol, HDL cholesterol, trigylcerides, Lp(a).

	1 **Tag X**	**2** **in the first year (= observation period)**	**3** **after 5-7 years**	**End of study**
Informed consent, inclusion/exclusion criteria	√			
Demographics	√	√	√	√
Medical history, AEs and SAEs	√	√	√	√
Concomitant medication, comorbidities	√	√	√	√
On-site pacemaker follow-up	√	√	√	
Start, discussion and optimization of telemedical monitoring (SMARTVIEW®).	√	√	√	
Venous blood draw		√§	√§	
TTE		√	√	
20 min risk ECG		√	√	
Questionnaires (EQ-5D-5L, ESS, STOP Bang)		√	√	
Ophthalmologic examinations		√ *	√ *	
Spirometry		√ *	√ *	
Angiological assessment (sonography, ABI)		√ *	√ *	


ACaSA
remote monitoring
respiratory disturbance index
daily activity
arrhythmias
CLIMATE effects: ambient temperature, humidity, air pressure, fine dust and pollen exposure
mean RDI, mean daily activity during first 12 months
RDI, daily activity during following years
assessment during first 12 months and after 5 years
questionnaires
biomarkers
TTE, sonography
biosignals
ophthalmo-logic exam
lung function test
PATIENT ALLOCATION DURING FIRST 12 MONTHS DETERMINANTS
sleep apnea (mean RDI < versus ≥ 20/h)
autonomic imbalance (PRD ≥ versus < 5.75 deg² in native and 3 deg² in paced QRS)
sedentary lifestyle (< versus ≥ mean 2h/d physical activity)
ACaSA CLIMATE
impact on DDAF and DDSA
ACaSA BIOMARKERS
impact on DDAF and DDSA
ACaSA OUTCOMES
1: TIME TO
3P-MACE (death, stroke, MI)
2: TIME TO
• unplanned CV hospitalisation
• CV death

ACaSA

ClinicalTrials.gov: NCT05127720