1 Title of the idea and proposing services

INTEGRA-HF Europe

Multimodal biomarkers with artificial intelligence for earlier detection and progression prediction of heart failure in primary care

Proposing services: Cardiology (Heart Failure Clinic, CLIC) and the ULSM primary care units (USF/UCSP), with DEFI-I&D (Research Department and OMOP data team). **Anchor project:** INTEGRA-CLIC trial, protocol v3.0.

2 Team

Lead: Prof. Cristina Gavina (Cardiology; MD, PhD, MSc Clinical Trials, Oxford). **Members:** Dr. Ana Sofia Correia (Cardiology, CLIC coordination); Dr. Fernando Montenegro Sá (Cardiology); Liliana Silva, RN, PhD (heart failure nursing and telemonitoring); Dr. Nuno Lourenço Silva (Data Scientist). **To be added:** a Family Medicine coordinator from the USF/UCSP units, a data scientist from the OMOP/DARWIN EU team, biostatistics and health economics support, and two patient representatives. Cardiology, family medicine, nursing, data science and health economics are thereby covered.

3 2027 topics addressed

Main: HORIZON-HLTH-2027-02-TOOL-01-two-stage, predictive biomarkers of disease progression and treatment response using AI in chronic non-oncological diseases (RIA; EUR 44.2 M; stage 1 on 17/02/2027, stage 2 on 16/09/2027). The proposal responds to the four expected outcomes (novel biomarkers, clinically validated biomarkers, trustworthy AI tools, better outcomes through clinical recommendations) and meets the scope conditions: high-quality clinical data already available, established AI methods, sex stratification, an EU-led prospective validation platform, a regulatory strategy and SME participation.

Alternative: HORIZON-HLTH-2027-02-DISEASE-01-two-stage, only if the project is reframed as an early-phase trial of a new intervention ("detect and treat": SGLT2 inhibitor initiated on an elevated NT-proBNP, followed by rapid nurse-led titration). The topic excludes comparative effectiveness studies and requires completed proof of concept, so a direct comparison between arms cannot be the core of the proposal.

4 Clinical problem

Heart failure (HF) affects 16.5% of the Portuguese population aged 50 and over; 90% of cases were undiagnosed, more than 90% have preserved ejection fraction and prevalence in women is twice that in men (21.0% vs 10.5%) [1]. In our population there are missed diagnostic opportunities in primary care before the first hospitalisation [2]. Isolated tests fail precisely where the problem is greatest: NT-proBNP falls by about 50 pg/mL for every 5 kg/m² of BMI, and fixed thresholds do not rule out HF in obesity [3]; AI-read ECG increases the diagnosis of reduced LVEF [4], but this is the minority phenotype. The problem is European: ageing, HFpEF, echocardiography waiting lists and therapies whose benefit emerges within weeks, which gives every month of delay a real prognostic cost.

5 Idea

Combine, using established AI methods, NT-proBNP, AI-read ECG, anthropometry (including waist-to-height ratio), laboratory and clinical data from the electronic health record and echocardiography into a multimodal biomarker that predicts the risk of progression from risk factors (stage A) to pre-HF (stage B), and from pre-HF to symptomatic HF (stage C) and hospitalisation, as well as the response to therapy initiated early.

- **Development on existing data:** ULSM OMOP records (about 318,000 people, 20 years of data), the PORTHOS cohort (6,189 participants with NT-proBNP, ECG and echocardiogram) and partner cohorts (Italy and Spain).
- **Prospective validation:** INTEGRA-CLIC (21 USF/UCSP units, about 94,500 eligible adults, three-arm cluster randomisation) serves as the platform, replicated in two to three countries; equity audit by sex, age, obesity and deprivation.
- **Translation:** decision support integrated into SClínico via FHIR, regulatory plan (MDR and AI Act, EMA scientific advice) and cost analysis per case identified and per QALY.

What changes: for patients, earlier diagnosis and treatment, in weeks rather than years; for family medicine, a targeted test that reduces unnecessary echocardiograms; for the Portuguese NHS (SNS), evidence ready for a national adoption decision. **ULSM's role:** clinical coordination of the consortium, or leadership of the clinical validation work package, with data and recruitment sites. **Partners:** HopeCare (Portuguese SME, electronic health record integration, agreement signed), an AI-ECG provider (SME, under negotiation), Abbott (point-of-care NT-proBNP, under negotiation); to be approached, European groups with NT-proBNP screening cohorts (Italy, Spain) and a European patient association. **Budget:** EUR 6 to 8 M per consortium; ULSM's share to be calibrated during mentoring, with the trial core already budgeted at EUR 686,400.

6 What already exists

INTEGRA-CLIC protocol v3.0 (August 2026) with study design, sample size calculation (81% power per comparison), statistical analysis plan and budget with and without in-kind contributions (EUR 246,200). CLIC in operation, with titration of the four pillars and telemonitoring. ULSM was the first Portuguese institution harmonised to the OMOP model and is a DARWIN EU Data Partner. NT-proBNP is reimbursed in primary care and a national clinical pathway has been published by the team [5]. Team publications on prevalence, natriuretic peptides and HF diagnosis [1-3,5,6].

[1] Baptista R et al. Eur Heart J 2026;47:4806-22 (PORTHOS). [2] Ferreira JP et al. ESC Heart Fail 2023;10:3438-45. [3] Gavina C et al. Eur J Heart Fail 2026, doi:10.1093/ejhf/xuag154. [4] Yao X et al. Nat Med 2021;27:815-9 (EAGLE). [5] Gavina C et al. Rev Port Cardiol 2026;45:591-9. [6] Santos M et al. Acta Med Port 2026;39:305-11. Topics: Funding & Tenders Portal, Work Programme 2026-2027, Cluster 1.