

Figure 1. Angiotensin Receptor Nephilysin Inhibitor (ARNI) and Sodium-Glucose Cotransporter-2 Inhibitor (SGLT2-i) distribution in the global population. Values are expressed as absolute numbers and percentages (%).

Parameter	Total	Enrolled	Not enrolled	Complicated
Age (years)	83,7±8,1	82,2±8,0	84,8±8,0	77,6±7,8
CIRS (points)	18,4±7,4	17,9±7,8	18,7±7,1	18,3±6,7
EF (%)	34,3±5,5	33,3±6,0	35,3±4,9	31,7±7,3
Creatinine (mg/dl)	1,82±0,96	1,44±0,44	2,09±1,12	1,56±0,42
eGFR (ml/min)	34±17	39±13	31±20	38±14
NT-proBNP (pg/ml)	11530	8990	13330	11830
NYHA (points)	3,04±0,70	3,02±0,68	3,06±0,71	3,50±0,65
Hospitalization (days)	9,1±4,1	8,8±4,0	9,3±4,3	9,7±4,6

Figure 2. Clinical features of the global population and of the subgroups (enrolled, not enrolled, and complicated patients during follow-up, that is, those who discontinued, were re-hospitalized, or died in follow-up). Continuous variables are reported as means (\pm Standard Deviation, SD).

CIRS, Cumulative Illness Rating Scale; EF, Ejection Fraction; eGFR, Estimated Glomerular Filtration Rate; NYHA, New York Heart Association Classification.

Disease	Total	Enrolled	Complicated
DM2	x	x	x
AF	x	x	
COPD	x	x	
Dyslipidemia	x	x	
Cancer	x		
Dementia	x		x
AOCP			x
Stroke			x
Parkinson			x
Cardiac arrest			x

Figure 3. Main comorbidities in the global population and in the subgroups. Those who discontinued were re-hospitalized, or died in follow-up had the most serious comorbidities in prognostic terms. COPD, Chronic Obstructive Pulmonary Disease; AF, Atrial Fibrillation; AOCP, Chronic Obstructive Obliterative Arteriopathy; DM2, Type-2 Diabetes Mellitus.

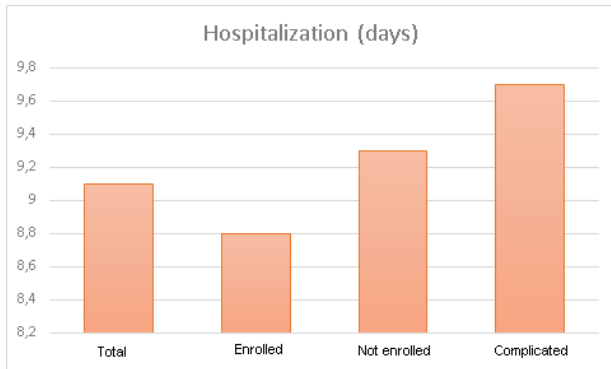


Figure 4. Length of the hospital stay. The whole enrolled group showed a hospitalization period of 8.8 days, the not-enrolled group 9.3 days, and those complicated in follow-up 9.7 days.

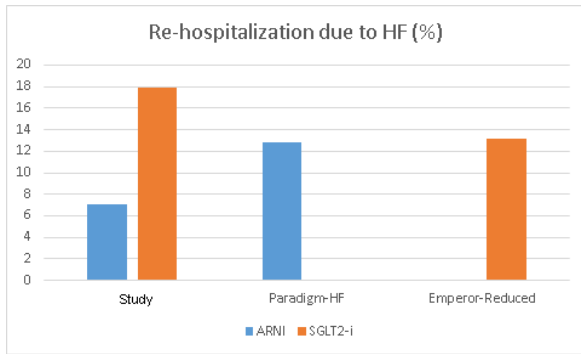


Figure 5. Re-hospitalizations for Heart Failure (HF) occurred in 7/34 patients (20.6%), of which 5/34 (14.7%) were for recurrent HF. There were 3 re-entries at 3 months and 2 re-entries at 6 months, *i.e.*, 7.1% in Angiotensin Receptor Inhibitor (ARNI) and 17.9% in Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2-i), while the Paradigm-HF trial registered 12.8%, and the Emperor-Reduced trial reported 13.2%.

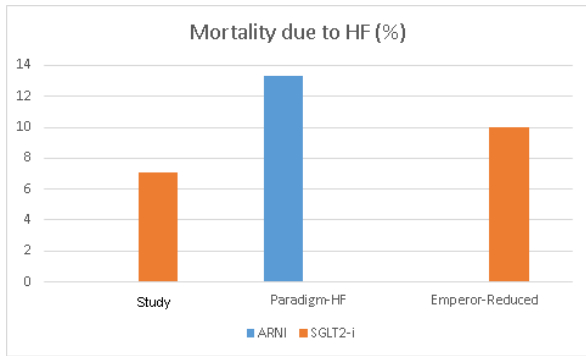


Figure 6. Mortality due to Heart Failure (HF). All-cause mortality occurred in 5/34 patients (14.7%), of which 2/34 (5.9%) due to recurrent HF; cardiovascular-cause mortality was registered twice: both patients were enrolled only with Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2-i) (7.1%). The Paradigm-HF registered 13.3% mortality, the Emperor-Reduced 10%.

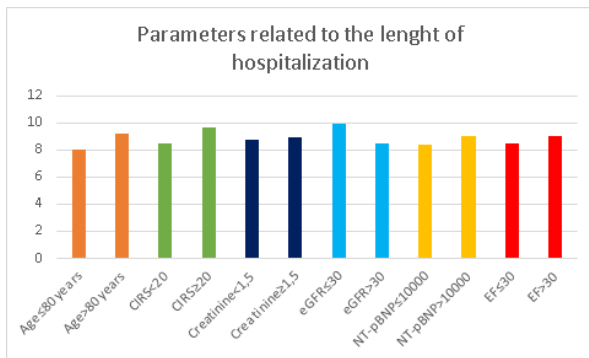


Figure 7. Parameters predicting the length of hospital stay. Age >80 years, eGFR ≤ 30 ml/min acc. Cockcroft-Gault, NT-proBNP on admission >10,000 pg/ml, CIRS score >20, personal history of cancer or dementia were confirmed as significant features, while EF didn't appear to be related to the lengthening of hospitalization (8.5 days if EF $\leq 30\%$, 9 days if EF >30%).

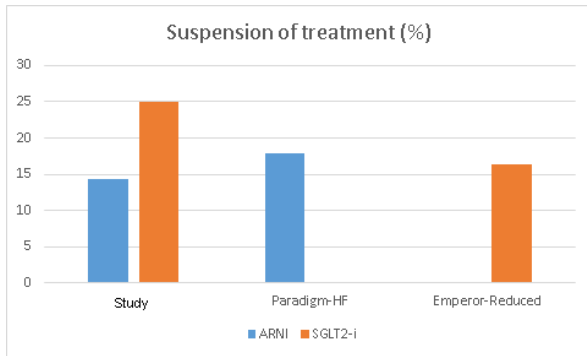


Figure 8. Patients who interrupted treatment with one or more drugs during follow-up. Overall, 9/34 (26.5%) were enrolled with Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2-i), 7/28 (25%) with Angiotensin Receptor Inhibitor (ARNI), and 2/14 (14.3%) with ARNI.

HF, Heart Failure.

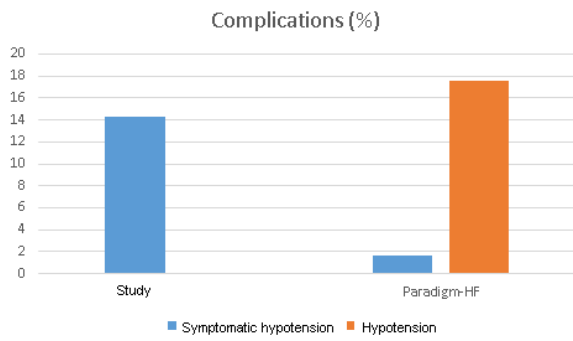


Figure 9. Incidence of complications (part 1). Symptomatic hypotension for Angiotensin Receptor Inhibitor (ARNI) was recorded in 2 women (14.3%). Literature data for sacubitril-valsartan showed hypotension in 17.6% of patients. See the text for further details.

HF, Heart Failure.

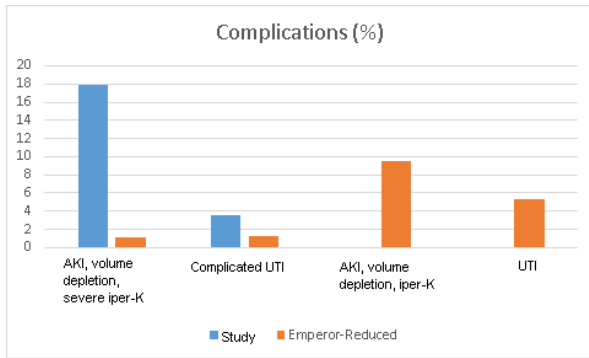


Figure 10. Incidence of complications (part 2). Severe acute kidney injury, volume depletion, and hyperkalemia occurred in 17.9% of Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2-i) enrollees; the literature reports a 9.5% incidence. Urinary Tract Infections (UTI) or complicated genital infections occurred in 3.6% vs 5.3% in the literature, which also considers uncomplicated infections. Severe hypoglycemia has never been recorded in line with Randomized Clinical Trials (RCTs). See the text for further details.

AKI, Acute Kidney Injury.