SGLT2 inhibitors in real-world patients with heart failure with preserved ejection fraction

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Introduction: The diagnosis and management of heart failure with preserved ejection fraction (HFpEF) is challenging since ejection fraction is normal, clinical signs are often lacking and there are few therapeutic options. Two randomized clinical trials have tested SGLT2i for the treatment of HFpEF: DELIVER (pending results) and EMPEROR-PRESERVED; the findings of the latter trial show that empagliflozin, a sodium-glucose co-transporter inhibitor (SGLT2i) reduces the risk of cardiovascular death or hospitalization for HF in patients with HFpEF regardless the presence of diabetes. The results of this clinical trial have allowed European Medicine Agency (EMA) to extend the indication also to the patients with HFpEF, however the characteristics of the trial population don't often correspond to real-word HF population.

Aims: This study aims to investigate the eligibility of the EMPEROR-PRESERVED and DELIVER trial to a real-world heart failure population comparing the baseline characteristics of our patients to the recruited patients of clinical trials.

Material and methods: In this retrospective, observational study, 206 HF outpatients were enrolled from September 2018 to September 2019. The percentages of eligible patients according to EMPEROR PRESERVED and DELIVER inclusion criteria were analyzed, then we analyzed the difference between the characteristics of our HFpEF population and trials population.

Results: 72 patients (35% of HF population) had heart failure with preserved ejection fraction. The EMPEROR-PRESERVED criteria and DELIVER trial were applied to these patients: 13 (18.1%) and 12 (16.7%) patients respectively fulfilled all enrolment criteria, whereas considering only EMA label criteria (EF >40% and eGFR >20 ml/min) 71 patients (98.6%) were eligible. The eligible patients according EMA criteria were significantly younger (67.3±14.3) than EMPEROR-PRESERVED population (72±9, p<0.001) and DELIVER population (72±10, p<0.001). The ejection fraction was significantly lower (50.2±5.8 vs 54±8.8; p<0.001) whereas eGFR was no significantly different (64.4±22.7 vs 60.6±19.8; p=0.17).

Conclusion: Only a small percentage of our heart failure with preserved ejection fraction population was eligible for SGLT2 inhibitors according trials criteria, whereas according to EMA label almost all patients are candidate to these drugs. Furthermore, these patients were younger than EMPEROR-PRESERVED and DELIVER population with lower EF. The difference of eligibility between trials and real population is related to inclusion criteria, in particular the trial patients had elevated NT-proBNP levels whereas in the real world this criterion isn't considered. There is a lack of data about real-world patients who are often different from trials population. National and international registries of HF population may resolve this issue.

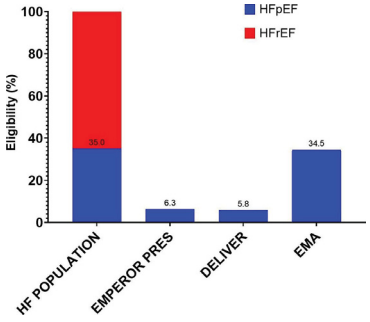

Figure 1. Eligibility of SGLT2i

Comparison of baseline characteristics in population with heart failure with preserved ejection fraction

	EMA label	EMPEROR PRESERVED	DELIVER
Age	67 ± 14	72 ± 9	72 ± 10
Women, %	31	45	44
NYHA functional class, %			
I	42,3	-	-
II	46,5	82	75
III	9,9	18	25
IV	1,4	0,3	0,3
Type 2 diabetes, %	18,3	49	45
Hypertension, %	60,6	90	89
AF at screening, %	19,7	35	42
LVEF, mean %	50	54	54
eGFR, mean ml/min/1,73 m^2	64	61	61
NT-proBNP, median, pg/ml	263	974	1011
ACEi, %	69	40	33
ARB, %	17	39	34
ARNI, %	1,4	2	4
MRA, %	28,2	37	39

Values are mean ± SD or n.
ACEi = angiotensin-converting enzyme inhibitor; AF = atrial fibrillation; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor-neprilysin inhibitor; eGFR= estimated glomerular filtration rate; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid receptor antagonist; NT-proBNP = N-terminal pro–B natriuretic peptide; NYHA = New York Heart Association.

Table 1. Baseline characteristics in population