81 Safety of sacubitril/valsartan in the elderly population with heart failure and reduced ejection fraction: a real-life observational study

Antonella Vincenzi[1], Matteo Casati[2], Antonio Cirò[3], Alessandra Annaloro[2], Federico Rea[2], Francesco Arace[4], and Maddalena Lettino[1]
[1]Cardiology, San Gerardo Hospital, Monza, Italy, [2]Internal Medicine, University of Milan-Bicocca, Monza, Italy, [3]Cardiology, Vimercate Hospital, Brianza, Italy, and [4]Department of Statistic, University of Milan-Bicocca, Monza, Italy

Aims: Prevalence of heart failure (HF) increases with age, but the elderly population is underrepresented in trials and the only data on the efficacy and safety of sacubitril/valsartan (S/V) in this group provided by the subanalysis of the PARADIGM trial, which confirms a favourable benefit-risk profile in all age groups. Information in a real-world setting is still lacking. Our study aims to evaluate the safety profile of S/V, in terms of risk of symptomatic hypotension, renal failure, and hyperkalaemia, in a group of real-life patients (pts) $>$ 75 years old (yo) presenting with HF and reduced Ejection Fraction (HFrEF).

Methods and results: 59 patients on S/V therapy older than 75 years (average age 78.9 $\pm$ 2.6) were identified out of a total number of 148 patients with HFrEF (39.8%), followed at our Heart Failure Clinic from December 2016 to April 2019. They were included in our retrospective observational cohort study. We compared their baseline characteristics (cardiovascular risk factors, mean serum creatinine, atrial fibrillation, EF) with the PARADIGM subgroup (1563pts, 18.6%) (average age: 79.1 $\pm$ 3.5) At time 0 (T0), and at 6 (T1), 12 (T2), and 18 (T3) months we assessed their serum creatinine, potassium and Nt-proBNP levels, blood pressure (BP), heart rate, NYHA class, eGFR (with MDRD), and the occurrence of death, hospital admissions for HF, symptomatic hypotension and angioedema. For the statistical analysis we used a marginal model with an unstructured covariance structure. Compared to the PARADIGM subgroup our study population showed a higher prevalence of AF (64.4% vs. 50.7%, *P* 0.039), a worse baseline creatinine (1.46 mg/dl vs. 1.22 mg/dl, $P < 0.001$) and eGFR (51.5 vs. 57.5 ml/min/1.73 m^2, *P* 0.005) (Figure 1). During the 18 months follow-up there was no significant increase in serum creatinine (*P* 0.092) and potassium (*P* 0.799). There was however a significant decrease in eGFR (from 51.46 to 45.36; *P* 0.015) and systolic BP (from 123.6 to 116.4 mmHg; *P* 0.021) and a higher rate of treatment discountination for symptomatic hypotension (5.1% vs. 1.8%, *P* 0.082) (Figure 2).

Conclusions: The present study confirmed the safety of S/V already shown in the PARADIGM trial, despite the worse baseline clinical characteristics of our elderly population. Our population had no significance increase in serum creatinine and potassium, similarly to the trial subgroup. Nevertheless there was a trend towards a higher rate of symptomatic hypotension leading more frequently to treatment discontinuation. Whether a more personalized implementation of S/V therapy in the ageing HF population (minimum starting dose, slower uptitration) would determine a higher tolerability of the drug should be specifically addressed by focused, prospective clinical trials.

	San Gerardo Hospital (n = 59)	Paradigm (n = 1563)	p value
Age, mean (SD)	78,9 (2,6)	79,1 (3,5)	0,664
Men, n (%)	48 (82.4)	1136 (72.7)	0,141
Hypertension, n (%)	48 (81,4)	1254 (80,2)	0,831
DM, n (%)	17 (28,8)	536 (34,3)	0,383
Atrial fibrillation, n (%)	38 (64,4)	793 (50,7)	0,039
SBP, mean (SD)	124 (19)	125 (16)	0,640
DBP, mean (SD)	72 (11)	72 (10)	1,000
HR, mean (SD)	67 (11)	71 (11)	0,006
Creatinine, mean (SD)	1,46 (0,39)	1,22 (0,32)	<0,001
GFR, mean (SD)	51,5 (16,7)	57,5 (16,0)	0,005
Ejection fraction, mean (SD)	27,6 (5,9)	30,9 (5,8)	<0,001

Baseline characteristics

	T0	T1	T2	T3	pvalue	tot
N	59	55	49	42		
SBP (mmHg), mean (SD)	123,6 (18,9)	118,6 (18,8)	118,1 (14,9)	116,4 (14,8)	0,021	
DBP (mmHg), mean (SD)	71,6 (10,9)	70,5 (8,9)	70,6 (8,3)	68,3 (7,2)	0,094	
HR (bpm), mean (SD)	66,9 (10,0)	68,1 (12,2)	67,9 (9,6)	68,8 (11,2)	0,779	
Creatinine (mg/dl), mean (SD)	1,46 (0,39)	1,48 (0,44)	1,67 (1,18)	1,64(0,50)	0,092	
Estimated GFR (mL/min/1,72m^2), mean (SD)	51,46 (16,45)	51,87 (19,17)	47,94 (15,36)	45,36 (16,33)	0,015	
Potassium (mEq/l), mean (SD)	4,59 (0,48)	4,54 (0,39)	4,62 (0,40)	4,62 (0,51)	0,799	
Syntomatic hypotension, n (%)		12 (22,2)	3 (6,1)	7 (16,7)		
Leading to discontinuation, n (%)		2 (3,6)	1 (2,0)	0 (0)		3 (5,1)
Death, n (%)		2 (3,6)	3 (6,1)	2 (4,8)		7 (11,9)
Sacubitril (mg/day)	78,1 ± 24,02	118,5 ± 49,6	120,0 ± 53,6	121,0 ± 53,6		

Results