Heart Failure

1 SACUBITRIL/VALSARTAN IN CHRONIC SYMPTOMATIC HEART FAILURE WITH REDUCED EJECTION FRACTION: FIRST CLINICAL EXPERIENCE FROM A LARGE UK TERTIARY CENTRE

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Introduction Sacubitril/valsartan (SV) is a new drug that has recently been approved by the National Institute for Health and Care Excellence (NICE) to be used as an alternative to ACE-inhibitors/Angiotensin Receptor Blockers in patients with symptomatic chronic heart failure with reduced ejection fraction (HFrEF). We report an early clinical experience of SV use in HF patients at a large tertiary cardiac centre in the UK.

Methods Patients with HFrEF (NYHA class II-IV and Left Ventricular Ejection Fraction <35%) seen in the heart failure clinic and started on Sacubtril/valsartan (one tablet 49/51 mg twice daily) from April till October 2016, were retrospectively evaluated. Change in NHYA class, eGFR, up-titration to target dose (one tablet 97/103 mg twice daily), deaths, hospitalizations and patients tolerability to SV were assessed. All patients had either their ACE-inhibitor or angiotensin receptor antagonist stopped at least 48 hours prior to starting sacubtril/valsartan and re-attended the HF clinic at 4 weekly intervals until up-titration was completed.

Results A total of 44 patients were commenced on SV and in 25 patients (57%) up-titration to the target dose was achieved. In 12 patients (27%) an improvement of NYHA class was seen. Nine patients (20%) had symptomatic systolic blood pressure drop of >10 mmHg at follow-up with 3 patients having hyperkalaemia (7%), preventing target dose up-titration. A total of 4 hospital admissions occurred: 2 due to decompensated heart failure (5%), 1 for hyperkalaemia and 1 non-cardiovascular (CV) related. Out of those hospital admissions, 2 patients died (see table). Four patients (9%) had a worsening of the eGFR>10 (without progressive renal failure preventing up-titration) and in 2 patients (5%) the drug was stopped to due intolerability (reported postural dizziness and abdominal pain).

Abstract 1 Table 1

Total number of patients commenced on sacubtril/valsartan	n=44
Male	36 (82%)
Average Age (years)	64 years
NYHA class improvement (≥1 class)	12 (27%)
Target dose up-titration achieved (97/103 mg)	25 (57%)
Drop of systolic Blood Pressure at follow-up (>10 mmHg)	9 (20%) 3 (7%)*
Hyperkalaemia (>6.0 mmol/L)	*(1 patient hospital admission due to hyperkalaemia)
Mortality and morbidity	2 (5%) in-hospital deaths* and 1 HF hospital admission *(1 due to progressive HF, 1 non CV-related hospital admission and death)
Sacubtril/valsartan intolerability and stopped	2 (5%) (reported dizziness and abdominal pain)
Deterioration in eGFR>10	4 (9%)

Conclusion The clinical use of SV in our centre has a high rate of tolerability with significant improvement in NYHA class (27%). However, in a large proportion of patients the target dose was not achieved (43%), mainly due to symptomatic hypotension and secondly due to hyperkalaemia (7%). A significant number of patients had a drop in eGFR, but this did not prevent up-titration. Our results confirm that HFrEF patients commencing sacubitril/valsartan require close monitoring of symptoms, renal function and dose titration by a specialist heart failure team.

2 SACUBITRIL/VALSARTAN: REAL WORLD EXPERIENCE OF DELIVERY AND TOLERABILITY

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Background Based on the PARADIGM-HF study trial, sacubitril/valsartan (SV) was approved by NICE in April 2016 (TA388) for patients with symptomatic heart failure. SV is recommended in patients with a left ventricular ejection fraction (LVEF) 35% despite a stable dose of ACE inhibitor (ACEi) or angiotensin receptor blocker (ARB), and large numbers are potentially eligible for this first-in-class drug. However, there is a lack of real world experience of both drug tolerability and systems for initiation and monitoring in overstretched heart failure services.

Methods Suitable patients were identified and started on SV by heart failure specialists. Dedicated, registrar-delivered monitoring and up titration clinics were established. Patients were reviewed 2–4 weekly. Symptoms, vital signs, biochemistry and hospital admissions were recorded at each visit. Once stable on optimal doses, patients were discharged to primary care, as pre-arranged with the District Prescribing Committee. Our initial 6 month experience has been analysed.

Results 69 patients (mean age 63.2±11.6 years) were commenced on SV. Mean LVEF 27.5±6.7%; mean baseline eGFR 66.1±21.9 ml/min/1.73m^2. Prior to initiation of SV, mean baseline ACEi/ARB dose was equivalent to 16.3±6.7 mg enalapril daily. Overall 68/69 (98.6%) prescriptions of SV were NICE TA388 compliant (1 patient ACEi/ARB intolerant).

9 patients (13.0%) stopped the medication due to adverse effects (PARADIGM-HF 17.8%), whilst another 3 patients (4.3%) were down titrated to a tolerable lower dose. 15.9% of all patients experienced symptomatic hypotension (PARADIGM-HF 14.0%). No episodes of angioedema, nor significant deterioration in renal function (50% reduction in eGFR) were observed. Only 1 (1.4%) patient was hospitalised with decompensated heart failure symptoms, but 3 (4.3%) patients were admitted with syncope secondary to orthostatic hypotension.

A total of 36 patients were discharged, with a median follow up time of 39 days (IQR 23) from commencement to stable discharge dose each requiring 1 initiation consultation and a mean of 2.4±1.0 follow up consultations. The majority of patients 25 (69.4%) were discharged at the highest dose – 97/103 mg BD. 23 (63.9%) of those discharged