timeframe, <10% of patients had SBP <100 mmHg and <5% K+ ≥6 mmol/L. A severely decreased eGFR (<30 ml/min/1.73m^2) was observed in 6–17%, while this was not correlated to sac/val titration patterns (Table).
Conclusions: The majority of patients were prescribed sac/val at the lowest dose and there were few attempts to up-titrate to the target dose during follow-up, while sac/val seems to be tolerated. Post-index measures of SBP, K+, and eGFR could not explain the lack of up-titration in the majority of patients. Educational efforts are warranted to ensure patients are treated to the maximum tolerated dose and achieve maximum benefit.
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Characteristics of heart failure patients treated with Sacubitril - Valsartan in Europe. Results from ARIADNE

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Background: Sacubitril/valsartan (S/V, LCZ696) reduces mortality and hospitalizations as compared to enalapril in patients with chronic heart failure with reduced ejection fraction (HFrEF). ARIADNE is a prospective registry describing the management of HFrEF and the way S/V is introduced by office-based cardiologists (OBCs) and primary care physicians (PCPs) in a real world setting.
Methods: HFrEF patients were included prospectively, independently of whether treatment had been changed recently or not. Here, we present baseline data from a first interim analysis of 3683 patients in 12 European countries.
Results: The characteristics of patients treated with s/V or standard of care (SoC) are shown in the table.

Table 1

	S/V	SoC	p-value
N	1896	1787	
Age in years (mean)	67.2	69.0	<0.01
Age ≥75 years (%)	31.9	36.7	<0.01
Female (%)	21.9	23.3	0.3
Ischemic etiology (%)	55.6	56.7	0.5
LVEF in % (mean)	32.2	34.5	<0.01
Beta blocker (%)	87.9	86.0	0.14
MRA (%)	64.0	53.1	<0.01
Loop diuretic (%)	67.6	59.7	<0.01
Cardiovascular device (%)	55.3	48.2	<0.01
NYHA III/IV (%)	56.4	31.7	<0.01
SBP in mmHg (mean)	127.0	128.5	0.06
Serum potassium in mmol/L (mean)	4.6	4.6	0.7
eGFR in ml/min (mean)	76.9	75.1	0.3

Conclusions: Early use of Sacubitril/Valsartan in European outpatients seems to be driven to a large extent by age, EF and symptoms with the majority of patients in NYHA classes III and IV. Safety measures like blood pressure, eGFR and potassium did not differ significantly in patients at the time of Sacubitril/Valsartan prescription.
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Heart rate reduction by selective sinus node blocker (ivabradine) protects against detrimental hemodynamic and structural effects of iv inotrops in heart failure

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Background: Short-term, infusion of inotropic agents are considered in symptomatically hypotensive / hypoperfused patients with heart failure (HF) decompensation. Such treatment brings immediate hemodynamic benefit and maintain vital organ perfusion / function. However Inotropes negatively influence failing heart as they exert detrimental effect on cardiomyocytes also unfavorably increase heart rate.
Aims: To determine the clinical, hemodynamic, structural effects of HR reduction (by HCN4 blockade – Ivabradine) in HF subjects, during iv inotropes treatment.
Methods: Male Wistar rats (n=100) were subjected to sham operation (ShO) or MI induction by ligation of the left anterior descending coronary artery. All animals underwent echocardiography 4 weeks after operation. ShO subjects presented normal whereas MI rats reduced left ventricle ejection fraction (LVEF <30%) so were defined as HF group. Both groups (ShO/HF) were further subdivided into 4 groups for 2-week infusion (subcutaneous Alzet osmotic pump): 1. dopamine (10 μg/min/kg), 2. ivabradine (10 mg/day/kg), 3. dopamine and ivabradine, 4. NaCl. At the end of the experiment echocardiography and pressure-volume (PV) loops were obtained, the rats were euthanized and the heart tissue was processed for biochemical testing.
Results: Neither rat died during 2 weeks experimental infusions. Dopamine infusion significantly increased HR both in ShO (442±23 bpm vs. NaCl 392±20, p<0.05) also HF rats (448±31 bpm vs. NaCl 405±23, p<0.05). Ivabradine reduced HR to a similar extend in both ShO and HF – alone/combined with dopamine (alone 315; combined 321 bpm, all p<0.05 vs. respective NaCl groups).
In HF group iv dopamine infusion resulted in significant left ventricular ejection fraction reduction (LVEF 17.8±2.2%), higher LV end-diastolic pressure (LVEDP 20.1±2.2 mmHg) and larger LV diastolic area (LVDA 98±10 mm^2), while ivabradine, given alone or in combination with dopamine, preserved the changes in these parameters (LVEF 22.2±2.0%, LVEDP 16.6±1.8 mmHg and LVDA 83±8 mm^2, respectively).
Conclusions: In chronic post MI HF, HR reduction with ivabradine prevents deleterious effects of dopamine infusion on LV hemodynamic and remodeling parameters. Thus HR control with ivabradine and its reduction during inotropic treatment could a viable therapeutic option in the setting of chronic heart failure.
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Beware of making dose comparisons for efficacy in post-hoc analyses of achieved dose in up-titrating studies: lessons from the EMPHASIS trial

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Background: Current heart failure (HF) guidelines recommend up-titration of angiotensin converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARBs), and beta-blockers to the maximum tolerated dose. There are currently no data to guide titration of mineralocorticoid receptor antagonists (MRAs). The present study aims to assess the prognostic implications of up-titrating eplerenone or matching placebo in the Eplerenone in Patients with Systolic Heart Failure and Mild Symptoms (EMPHASIS-HF) trial.
Methods: In EMPHASIS-HF eplerenone was maintained at 50 mg/day or 25 mg/day if the estimated glomerular filtration rate (eGFR) was 30 to 49 ml/min/1.73 m^2. The primary outcome was a composite of heart failure hospitalization (HFH) and cardiovascular mortality (CVM). Cox proportional hazard regression models were used to model long-term event rate.
Results: Compared to patients who could not be up-titrated, patients up-titrated to eplerenone or placebo dose ≥25 mg/d were younger, had better renal function, higher hemoglobin, had fewer previous HFH and less implanted devices (p<0.05 for all). Patients up-titrated to higher eplerenone doses had better prognosis compared to patients assigned to lower doses, adjusted HR (95% CI) for the primary outcome of HFH or CVM ≈0.6 (0.5–0.8) for both eplerenone and placebo groups, with similar findings observed for the individual components of the primary outcome.
Conclusion: The present study shows that patients who could be up-titrated, whether on eplerenone or placebo, had a less severe clinical profile. Therefore, this type of post-randomization dose titration sub-group analysis is inappropriate for examining whether higher doses are more effective than lower doses in a clinical trial. It cannot reject this hypothesis, either. The selection of lower risk patients for higher treatment doses induces a prognostic association bias. Therefore, further prospective studies will be required to determine the optimum dose of eplerenone
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Tolerability and safety of sacubitril/valsartan in high-risk subgroups

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Introduction: Current ESC guidelines recommend sacubitril/valsartan (SV) for patients (P) with ongoing symptomatic chronic heart failure with reduced ejection fraction, despite first line medical therapy. Experience regarding tolerability and safety in real world is less well described, mainly in high-risk subgroups.
Purpose: To assess tolerability and success in achieving maximum SV dose in high-risk subgroups of a real world population.
Methods: Retrospective and descriptive study extended to all P initiated and up-titrated on SV in a specialized HF unit since October 2016. P were stratified as high-risk if: systolic blood pressure (SBP) <110mmHg, pre-study low