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Have we found the Holy Grail in Heart failure with reduced ejection fraction? - First experiences with sacubitril/valsartan among heart transplant candidates

Authors:
B Muk1, D Vagany1, P Bogyi1, D Pilecky2, ZS Majoros1, M Dekany1, T Borsanyi1, B Polgar1, K Kosa1, E Szogi1, I Juhasz1, LCS Nyeki3, RG Kiss1, N Nyolczas1, 1Medical Centre, Hungarian Defence Forces, Cardiology - Budapest - Hungary, 2Klinikum Passau, Internal Medicine and Cardiology - Passau - Germany, 3Semmelweis University - Budapest - Hungary,

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Background: Heart failure is even today a life-limiting disease throughout the world. Mortality and morbidity of heart failure with reduced ejection fraction (HFrEF) is comparable with malignancies, despite the available pharmacological and non-pharmacological treatment possibilities. Over the last few years, a new, very promising family of substances – angiotensin receptor neprilysin inhibitors (ARNi) – has appeared. Sacubitril/valsartan, first-in-class of ARNi, has been proven effective, surpassing all expectations in a PARADIGM HF study published in 2014. Based on the evidence from this study, the current ESC guidelines for the diagnosis and treatment of acute and chronic heart failure published in 2016 recommend the use of the drug for stable HFrEF patients. However the drug became available worldwide very recently.

Cases: We report the cases of 9 patients (NYHA: 3.3±0.5; LVEF: 26.2±3.7%; age: 51.3±13.7years; male: 88.9%; ischemic: 55.6%; atrial fibrillation: 33.3%; diabetes: 11.1%; systolic blood pressure: 103.9±8.3mmHg; eGFR: 54.3±16.1ml/min/1.73m²) who were suffering from advanced HFrEF in spite of optimized therapy (ACEi/ARB: 100%; at target dose (TD) of ACEi/ARB: 55.5%; BB: 100%; at TD of BB: 77.8%; MRA: 100%; ICD: 100%; CRT-D: 22.2%) and were referred to our heart failure clinic for heart transplantation (HTx) evaluation. After baseline non-invasive (6 minute-walking test (6MWT), cardiopulmonary exercise test) and invasive evaluation (right heart catheterization) for heart transplantation (NTproBNP: 3608.5±2375.5pg/ml; peakVO2: 11.1±2.1ml/kg/min; 6MWT: 424.2±162.9m; CI: 1.83±0.44l/min/m²) sacubitril/valsartan was initiated and successfully titrated to the maximal tolerated level (275mg±116.5mg/die). After 3 months of follow-up the non-invasive and invasive tests were reapplied showing significant improvement in the clinical condition (NTproBNP: 1589.9±692.9pg/ml; peakVO2: 13.8±3.31ml/kg/min; 6MWT: 500.7±71.5m; CI: 2.91±0.11/min/m²). Based on these results only 3 out of 9 patients remained eligible for HTx and were referred to the HTx Committee.

Conclusions: HFrEF even nowadays is a deadly disease. In case of its progression in spite of optimized therapy and without the presence of any contraindication, HTx should be performed. However the time on the waiting list can be quite long, potentially resulting several complication. Based on our preliminary experience, with sacubitril/valsartan as part of a complex heart failure treatment, significant improvement could be achieved even among HTx candidates, which improvement in the clinical status could make the HTx temporary unnecessary or the time on the waiting list safer.