

## HEART FAILURE

# Neprilysin inhibition attenuates risk of hyperkalaemia in HFrEF

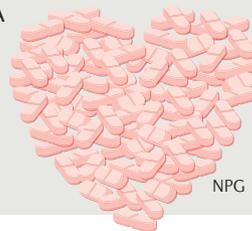
In patients with heart failure and reduced ejection fraction (HFrEF), neprilysin inhibition with sacubitril/valsartan might attenuate the increased risk of hyperkalaemia that occurs when mineralocorticoid receptor antagonists (MRAs) are used in combination with other renin-angiotensin-aldosterone system inhibitors. This secondary analysis of the PARADIGM-HF trial was presented at the AHA Scientific Sessions 2016 and simultaneously published in *JAMA Cardiology*.

In patients with symptomatic HFrEF, the use of MRAs can reduce the risk of death or hospitalization. However, MRA use is also associated with a heightened risk of hyperkalaemia, especially in patients with chronic kidney disease. In their primary analysis, investigators of the PARADIGM-HF trial reported that patients with HFrEF who

received sacubitril/valsartan showed lower rates of death and hospitalization than those who received enalapril. In the present secondary analysis, the investigators sought to determine whether sacubitril/valsartan can reduce the risk of hyperkalaemia associated with MRA use in patients enrolled in the PARADIGM-HF study.

Among 8,399 patients enrolled in the trial, 4,671 (55.6%) were taking an MRA at baseline. These patients were younger, had a lower ejection fraction, and more advanced heart failure symptoms than those not treated with an MRA. Among patients taking an MRA at baseline, the rates of hyperkalaemia were similar in both treatment groups, but severe hyperkalaemia was more common in patients receiving enalapril than in those receiving sacubitril/valsartan (3.1 versus 2.2 per

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100 patient-years; HR 1.37, 95% CI 1.06–1.76,  $P=0.02$ ). Among patients who had just begun taking MRAs upon enrolment into the PARADIGM-HF trial, severe hyperkalaemia also occurred more frequently in those receiving enalapril than in those receiving sacubitril/valsartan.

“The use of sacubitril/valsartan in preference to enalapril among eligible patients with HFrEF may enhance the ability to use MRAs safely, allowing patients to reap the incremental benefits at less incremental risk,” conclude the PARADIGM-HF investigators. “These observations provide additional rationale to consider replacing [angiotensin-converting-enzyme] inhibitors with sacubitril/valsartan for suitable patients in clinical practice.”

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**ORIGINAL ARTICLE** Desai, A. S. *et al.* Reduced risk of hyperkalemia during treatment of heart failure with mineralocorticoid receptor antagonists by use of sacubitril/valsartan compared with enalapril: a secondary analysis of the PARADIGM-HF trial. *JAMA Cardiol.* <http://dx.doi.org/10.1001/jamacardio.2016.4733> (2016)

**FURTHER READING** von Lueder, T. G. & Krum, H. New medical therapies for heart failure. *Nat. Rev. Cardiol.* **12**, 730–740 (2015)