

Novartis heart-failure med Entresto cuts A1c

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Novartis announced results of a new post-hoc analysis in a subgroup of patients with reduced ejection fraction heart failure (HFrEF) and diabetes suggesting that Entresto (sacubitril/valsartan) tablets improved glycemic control, as assessed by hemoglobin A1c (HbA1c) testing, compared to ACE-inhibitor enalapril.

HFrEF is also known as systolic heart failure (HF). Entresto is indicated to reduce the risk of cardiovascular (CV) death and hospitalization for HF in patients with chronic HF (NYHA Class II-IV) and reduced ejection fraction. It is not indicated to treat diabetes.

Entresto lowered HbA1c levels - a measure of average blood glucose levels for the past two to three months - after one year of treatment for HF, and this effect was sustained over three years of study follow-up¹. In the analysis, new use of insulin therapy or oral diabetes agents was also reduced in the Entresto group. The findings are based on data from PARADIGM-HF, the largest clinical trial ever conducted in HF⁵, and are simultaneously being presented today at the American College of Cardiology (ACC) 66th Annual Scientific Session & Expo in Washington, D.C. and published in *The Lancet Diabetes & Endocrinology*.

"Diabetes is a major risk factor in heart failure and is strongly linked to progression of the disease, putting heart failure patients at increased risk of hospitalization and death," said Scott Solomon, MD, Director of Noninvasive Cardiology, Brigham and Women's Hospital, Professor of Medicine, Harvard Medical School, and senior author of the publication. "This analysis suggests that, in addition to the proven heart failure benefits demonstrated in PARADIGM-HF, Entresto may also help tighten glycemic control among heart failure patients with diabetes."

An analysis was conducted of 3,778 HFrEF patients in the PARADIGM-HF trial who were diagnosed with diabetes or had a

baseline HbA1c \geq 6.5% without a reported diagnosis at screening (98% of patients assessed had type 2 diabetes). The investigators compared the effects of Entresto vs. enalapril on glycemic control by measuring patients' HbA1c levels at screening and at one-, two-, and three-year follow-up visits, and by evaluating patients' initiation of oral antihyperglycemic or insulin therapy during the study.

This post-hoc analysis found that Entresto decreased HbA1c levels by 0.26% during the first year of follow-up, compared to a 0.16% reduction with enalapril ($p=0.0023$)¹. Over three years, HbA1c levels remained persistently lower in patients treated with Entresto compared to enalapril, with an overall reduction of 0.14% (95% CI [0.06, 0.23]; $p=0.0055$)¹. In addition, 29% fewer Entresto-treated patients initiated insulin therapy to achieve glycemic control (114 (7%) vs. 153 (10%) patients, HR 0.71, 95% CI, 0.56-0.90; $p=0.0052$)¹. Entresto was shown to reduce the risk of CV death or HF hospitalization compared with enalapril among patients with or without diabetes at baseline^{1,6,7}.

"On top of the already well-demonstrated clinical benefits of Entresto, a reduction in HbA1c levels in these type 2 diabetes patients is of great interest and shows us that further research is needed to better understand this metabolic effect of the drug," said Fabrice Chouraqui, President of Novartis Pharmaceuticals Corporation. "Novartis is committed to exploring the full potential of this important medication to maximize its value for heart failure patients managing their chronic condition."