

Title of Research

Changes in Renal Function with Neprilysin Inhibition versus Angiotensin Converting Enzyme Inhibition in Patients with Heart Failure

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Summary of Research

There has been interest in changes in kidney function during treatment of acute and chronic heart failure. Initially, it was thought that all worsening kidney function (also known as worsening renal function or WRF) was associated with poor outcomes. However, it is now clear that WRF in the setting of heart failure status improvement or stabilization is not associated with poor outcomes. Retrospective analyses of large trials of drugs that inhibit the renin angiotensin aldosterone system (RAAS) – involved in regulating plasma sodium levels and arterial blood pressure – have also shown that WRF during initiation of RAAS inhibitors is not associated with higher mortality risk, in contrast to WRF that occurs with placebo.

A novel angiotensin receptor neprilysin inhibitor (ARNI) has been shown to improve outcomes in patients with chronic heart failure compared with enalapril, an angiotensin converting enzyme (ACE) inhibitor. This novel compound showed less WRF and less elevation in blood levels of potassium (hyperkalemia), and patients also discontinued therapy at a lower rate.

With the recent renewed interest in combined neprilysin inhibition in combination with RAAS inhibition, the OVERTURE trial (Omapatrilat vs Enalapril in Heart Failure) gives important insights into how neprilysin inhibition by omapatrilat (is a dual inhibitor of ACE and neutral endopeptidase) differs from enalapril (ACE inhibitor). Since there are only limited number of studies investigating neprilysin inhibition in heart failure, and only two outcome trials to date (of which OVERTURE is one), using the data gathered by OVERTURE could be helpful in determining the pros and cons of this therapy in terms of renal function and associated outcomes.

Study Design

The objectives of the proposed analysis are to: a) evaluate and compare the changes in kidney function with omapatrilat versus enalapril; b) evaluate and compare the incidence of WRF with both therapies; and c) evaluate the differential relationship between the occurrence of WRF with omapatrilat vs. enalapril and the association with outcomes. A retrospective analysis of the OVERTURE dataset will be carried out, with a descriptive analysis of the changes in renal function during initiation of therapy and later. The incidence of WRF in both treatment groups will be assessed by changes in serum creatinine levels. The primary outcome will be the first occurrence of cardiovascular death or heart failure hospitalization, with secondary outcomes including each individual component and all-cause mortality.

Study Population

The analysis will include the OVERTURE population, totaling 5,770 participants, who have at least two serum creatinine measurements and outcomes available.

Funding Source of Research

N/A

Requested Study

CV137-068: Omapatrilat versus Enalapril, Randomized Trial of Utility in Reducing Events (OVERTURE)