

# Combination therapy for heart failure does not reduce risk of CV death or rehospitalization

March 11 2013

---

Among patients hospitalized for heart failure (HF) with reduced left ventricular ejection fraction (LVEF; a measure of how well the left ventricle of the heart pumps with each contraction), initiation of the medication aliskiren in addition to standard therapy did not reduce cardiovascular death or HF rehospitalization at 6 or 12 months after discharge, according to a study published online by *JAMA*.

"Inhibition of the renin-angiotensin-aldosterone system [RAAS; the regulation of sodium balance, fluid volume, and blood pressure by secretion of renin in response to reduced [perfusion](#) of the kidney] has long been recognized as a life-prolonging therapy for patients with [chronic heart failure](#) with reduced LVEF, and angiotensin-converting enzyme (ACE) inhibitors, angiotensin II [receptor blockers](#) (ARBs), and mineralocorticoid [receptor antagonists](#) (MRAs) are recommended by all major national guidelines. However, although the benefits of these treatments are undisputed, these agents induce a compensatory increase in renin [an enzyme secreted by the kidneys] and downstream RAAS intermediaries that may partially offset RAAS blocking effects," according to background information in the article.

The direct renin inhibitors (DRIs) represent another pharmacologically distinct method for RAAS blockade. Aliskiren, an orally active DRI, has demonstrated a favorable hemodynamic and neurohormonal profile in patients with HF. "Despite current evidence-based therapies, patients

with hospitalization for HF (HHF) face postdischarge mortality and rehospitalization rates as high as 15 percent and 30 percent, respectively, within 60 to 90 days. Incomplete suppression of the RAAS may contribute to the exceptionally high postdischarge event rate," the authors write.

Mihai Gheorghiade, M.D., of the Northwestern University Feinberg School of Medicine, Chicago, and colleagues conducted a study (the ASTRONAUT randomized trial) to examine whether the addition of a DRI (aliskiren) to standard therapy would improve long-term outcomes in HHF patients. The study included hemodynamically stable HHF patients a median (midpoint) 5 days after admission who met certain criteria. Patients were recruited from 316 sites across North and South America, Europe, and Asia between May 2009 and December 2011. The follow-up period ended in July 2012.

All patients received 150 mg (increased to 300 mg as tolerated) of aliskiren or placebo daily, in addition to standard therapy. The study drug was continued after discharge for a median 11.3 months.

The final group for efficacy analyses included 1,615 patients (808 assigned to aliskiren, 807 assigned to placebo). At randomization, patients were receiving diuretics (95.9 percent), beta-blockers (82.5 percent), [ACE inhibitors](#) or ARBs (84.2 percent), and MRAs (57.0 percent). There were no major differences between the 2 treatment groups at the time of randomization. The average age was 65 years.

"In total, 24.9 percent of patients receiving aliskiren (77 cardiovascular [CV] deaths, 153 HF hospitalizations) and 26.5 percent of patients receiving placebo (85 CV deaths, 166 HF rehospitalizations) experienced the primary end point [[cardiovascular death](#) or HF rehospitalization] at 6 months. At 12 months, the event rates were 35.0 percent for the aliskiren group (126 CV deaths, 212 HF

rehospitalizations) and 37.3 percent for the placebo group (137 CV deaths, 224 HF rehospitalizations)," the authors write.

During the overall follow-up period (ranging from 0.1 to 31.2 months), the total hospitalization rates (i.e., percentage of patients hospitalized for any reason) in the aliskiren and placebo groups were 48.1 percent and 49.1 percent, respectively. The HF hospitalization rates within 12 months were 26.2 percent in the aliskiren group and 27.8 percent in the placebo group.

The researchers also found that the rates of hyperkalemia (higher than normal levels of potassium in the circulating blood), hypotension, and renal impairment/renal failure were higher in the aliskiren group compared with placebo.

"The results of the ASTRONAUT study do not support the routine administration of aliskiren, in addition to evidence-based therapy, to patients hospitalized for worsening chronic HF. Subgroup analysis is consistent with previous reports of poor outcomes with the use of aliskiren in patients with diabetes mellitus [DM] already taking RAAS inhibitors. Further investigations are needed to evaluate the effects of renin inhibition in a large cohort of HHF patients that excludes [patients](#) with DM," the authors conclude.

**More information:** [doi:10.1001/jama.2013.1954](https://doi.org/10.1001/jama.2013.1954)

The study is being released early to coincide with its presentation at the American College of Cardiology's annual Scientific Sessions.

Provided by JAMA and Archives Journals

Citation: Combination therapy for heart failure does not reduce risk of CV death or rehospitalization (2013, March 11) retrieved 4 May 2024 from <https://medicalxpress.com/news/2013-03-combination-therapy-heart-failure-cv.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.