

High-Dose Is Better Than Low-Dose Losartan in Some Patients with CHF

Up-titration provided clinical benefit.

In several studies, high-dose angiotensin-receptor blockers (ARBs), either alone or in combination with angiotensin-converting-enzyme (ACE) inhibitors, have lowered cardiovascular morbidity and mortality in patients with congestive heart failure and reduced left ventricular ejection fraction (LVEF). Because the effects of different ARB dosing regimens are unknown, manufacturer-sponsored researchers randomized 3846 patients with NYHA class II–IV CHF, LVEF \leq 40%, and intolerance to ACE inhibitors to receive losartan up-titrated to either 50 mg or 150 mg daily. Most patients received other standard therapies, including β -blockers.

After a median 4.7 years of follow-up, patients who were taking high-dose losartan were significantly less likely to reach the composite primary endpoint (hospitalization for heart failure or death) than were those in the low-dose group (11.1 vs. 12.4 events per 100 patient-years). High-dose patients had significantly fewer cardiovascular and heart-failure admissions than did low-dose patients, but differences in all-cause and cardiovascular mortality were not significant. Patients who were taking high-dose losartan experienced significantly more hyperkalemia, hypotension, renal impairment, and angioedema than did low-dose patients, but researchers found no significant differences between groups in adverse events leading to drug discontinuation.

Comment: This trial adds to accumulating evidence suggesting that higher doses of ARBs incrementally inhibit angiotensin-receptor activity, with potentially improved clinical outcomes but with more adverse effects. But these conclusions cannot be extended to patients who tolerate ACE inhibitors or who are taking them concomitantly nor does it suggest that ARBs are more effective than ACE inhibitors in this setting.

— [Bruce Soloway, MD](#)

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Konstam MA et al. Effects of high-dose versus low-dose losartan on clinical outcomes in patients with heart failure (HEAAL study): A randomised, double-blind trial. *Lancet* 2009 Nov 28; 374:1840.