BACKGROUND: The basis for expectation of significant benefit for angiotensin II blockade is that angiotensin levels are inadequately blocked over 24 hours with ACE inhibitor therapy alone at recommended doses.

PURPOSE: Val-HeFT was undertaken to examine the effect on morbidity and mortality, in a large-scale, double-blind, placebo-controlled trial, of the selective angiotensin receptor blocker valsartan versus placebo, in addition to usual therapy with ACE inhibitors, beta blockers, diuretics, and digoxin.

PATIENT POPULATION: Patients were men (n=4,005) and women (n=1,005) 18 years or older (mean age 62) with mild to severe chronic heart failure (New York Heart Association [NYHA] class II: 62%; NYHA class III: 36%; NYHA class IV: 2%) and ejection fraction <40%. About 57% had heart failure of ischemic origin.

METHODS: Patients were randomized to either valsartan titrated to a target dose of 160 mg b.i.d. (n=2,511) or placebo (n=2,499) while continuing other appropriate therapies. These included ACE inhibitors in 93% of patients, beta blockers in 36%, diuretics in 86%, and digoxin in 67%. The primary endpoints were all-cause mortality (time to death) and combined all-cause mortality and morbidity (time to event). Morbid events included sudden death with resuscitation, hospitalization for heart failure, and need for therapeutic doses of intravenous inotropic or vasodilating agents for at least 4 hours. Patients were evaluated for approximately 2 years.

RESULTS: All-cause mortality was similar between groups at 19.7% for valsartan and 19.4% for placebo. Combined all-cause mortality plus morbidity, however, was reduced by 13.3% in the valsartan group to a highly significant degree (28.8 vs. 32.1%, p=0.009). Reductions in heart failure hospitalizations (27.5%), and improvements in NYHA functional class (22.9%), ejection fractions, signs and symptoms, and quality of life were all significant with valsartan therapy. The benefit of valsartan on mortality and morbidity was particularly prominent in patients who were not taking beta blockers. There was increased risk for adverse events in patients taking both an ACE inhibitor and a beta blocker, but not in patients taking either an ACE inhibitor or a beta blocker. The rate of discontinuations was slightly higher in the valsartan group than in the placebo group (9.9 vs. 7.2%), most commonly because of dizziness, hypotension, or renal impairment.

CONCLUSION: Valsartan is an effective therapy to reduce combined morbidity and mortality in patients receiving usual therapy for heart failure.