
CONTEXT: Results from recent studies on the effects of beta1-blockade in patients with heart failure demonstrated a 34% reduction in total mortality. However, the effect of beta1-blockade on the frequency of hospitalizations, symptoms, and quality of life in patients with heart failure has not been fully explored.


DESIGN: Randomized, double-blind controlled trial, preceded by a 2-week single-blind placebo run-in period, conducted from February 14, 1997, to October 31, 1998, with a mean follow-up of 1 year.

SETTING: Three hundred thirteen sites in 14 countries. PARTICIPANTS: Patients (n = 3991) with chronic heart failure, New York Heart Association (NYHA) functional class II to IV, and ejection fraction of 0.40 or less who were stabilized with optimum standard therapy.

INTERVENTIONS: Patients were randomized to metoprolol CR/XL, 25 mg once per day (NYHA class II), or 12.5 mg once per day (NYHA class III or IV), titrated for 6 to 8 weeks up to a target dosage of 200 mg once per day (n = 1990); or matching placebo (n = 2001).

MAIN OUTCOME MEASURES: Total mortality or any hospitalization (time to first event), number of hospitalizations for worsening heart failure, and change in NYHA class, by intervention group; quality of life was assessed in a substudy of 741 patients.

RESULTS: The incidence of all predefined end points was lower in the metoprolol CR/XL group than in the placebo group, including total mortality or all-cause hospitalizations (the prespecified second primary end point; 641 vs 767 events; risk reduction, 19%; 95% confidence interval [CI], 10%-27%; P < .001); total mortality or hospitalizations due to worsening heart failure (311 vs 439 events; risk reduction, 31%; 95% CI, 20%-40%; P < .001), number of hospitalizations due to worsening heart failure (317 vs 451; P < .001); and number of days in hospital due to worsening heart failure (3401 vs 5303 days; P < .001). NYHA functional class, assessed by physicians, and McMaster Overall Treatment Evaluation score, assessed by patients, both improved in the metoprolol CR/XL group compared with the placebo group (P = .003 and P = .009, respectively).

CONCLUSIONS: In this study of patients with symptomatic heart failure, metoprolol CR/XL improved survival, reduced the need for hospitalizations due to worsening heart failure, improved NYHA functional class, and had beneficial effects on patient well-being.