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Carvedilol®, a β-blocker with vasodilating properties via α1-blockade, was evaluated in patients with severe chronic heart failure (CHF) [ejection fraction (EF) ≤ 0.35, NYHA III/IV] in a double-blind, placebo-controlled trial of 6 months duration. The protocol was stopped early upon recommendation of the Data and Safety Monitoring Board to terminate Phase III clinical trials in light of a survival advantage of C. One-hundred five of a planned 140 patients on standard therapy (diuretics, digoxin, and ACE-I) and unable to walk 350 m in 6 min were randomized to receive maximally tolerated C (n=70) up to 25 mg bid or placebo (P; n=35). Parameters evaluated included change in quality of life (Minnesota Living with Heart Failure Questionnaire), patient/Physician global assessment and EF. Analyses (at end-point) were limited to 40 patients on C and 21 on P, due to truncation of the study.

Results: Patients receiving C had a greater increase in EF at 6 months compared to P (+0.09 vs +0.02; p=0.004). Clinical benefit was evidenced by improvement in the global assessment by patients in 88% on C vs 67% on P (p=0.032), and by physicians in 83% vs 52% (p=0.023). Only 3% of patients/physicians reported worsened CHF on C, whereas 19% patients and 15% physicians reported worsened CHF on P. Two deaths (2.9%) occurred on C and Two (5.7%) on P. Several other measures of efficacy favored C without reaching statistical significance, including change in quality of life score (+12 C; +9 P), 6-min walk distance (299.9 m on C, 278.3 m on P), improvement in NYHA Class (23% C vs 19% P). Hospitalizations for worsening CHF occurred in 7.5% of patients on C, and 4.8% on P.

Conclusion: The addition of carvedilol to diuretics, digoxin and ACE-I therapy in patients with severe CHF results in an improvement in EF and reduced risk of clinical deterioration. These data are concordant with the homodynamic and clinical benefits observed in patients with less severe CHF treated with carvedilol.