Effect of controlled-release metoprolol on total mortality, hospitalizations, and well-being in patients with heart failure: Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure

MERIT-HF Study Group. JAMA 2000;283:1295-1302 (March 8)

Study Type: POEM
Study Duration: follow-up mean 1 year, study was stopped early
Patients: 3991 patients, mean age 64 years, 78/22-male/female, 94% white, 41%/56%/3%-Class II/III/IV, ~90-95% of patients on ACE inhibitor and diuretic, ~64% on digoxin, 7% on spironolactone

Trial Design: Double-blinded, placebo-controlled, randomized, intention-to-treat, multicenter (313 hospitals, 13 countries), placebo verses metoprolol CR/XL dose titration

Purpose: Does long-acting metoprolol reduce frequency of hospitalizations, symptoms, and quality of life in patients with Class II/III/IV HF? Total mortality arm of this study was published in Lancet.

Inclusion: Symptomatic heart failure (class II-IV), measured EF < 40% within 3 months, must be stable during 2 week placebo run-in, those with EF of 36-40% were included only if their 6 min walking test was < 450 m.

Exclusion: acute MI, unstable angina within 28 days of study, CI to beta-blocker therapy, other drugs with beta-blocking effects like amiodarone, beta-blocker use for other indications, use within 6 weeks of enrollment, HF from alcohol abuse, scheduled heart transplant, implanted defibrillator, CABG, PTCA within 4 mths, second or third degree heart block, unstable HF, low BP (systolic < 100), use of amiodarone, dilt, verapamil within 6 mths

Outcome Events: Primary endpoints: All-cause mortality, (used independent committee) all-cause mortality + all-cause admission to hospital.
Other endpoints: total mortality + hospitalization due to worsening HF, death or transplantation, cardiac death or nonfatal MI,

1. Are the results valid?
   * randomized? yes
   * double-blinded? yes
   * placebo run in? yes
   * were groups similar? yes
   * all patients accounted for? yes

2. What were the results?
   
   Primary endpoint: placebo metoprolol RRR ARR P value NNT
   Total mortality or all-cause hospitalization 38.3% 32.2% 19% 6.1% <.001 16
   Total mortality or hospitalization due to worsening HF 22.0% 15.6% 31% 6.4% <.001 16
   Death or transplantation 10.9% 7.5% 32% 3.4% <.001 29
   Cardiac death or nonfatal MI 11.2% 7.0% 39% 4.2% <.001 24
   Total mortality or hospitalization or ER visits due to worsening HF 22.7% 16.0% 32% 6.7% <.001 15
   
   Hospitalizations alone
   all-cause 33.3% 29.1% 18% 4.2% .004 24
   due to cardiovascular causes 24.7% 19.8% 25% 4.9% <.001 20
   due to worsening HF 14.7% 10.0% 35% 4.7% <.001 21

3. Will the results help me?
   * 2090 days saved from all-cause hospitalizations (p=.004), 1902 hospital days saved due to worsening HF
   * more favorable change in NYHA class with the metoprolol group
   * 50% (40% in placebo gr) of those taking QOL questions reported improvement and 72% judged this change to be important
   * no significant side effect differences, fewer than 1/100 withdrew due dizziness, bradycardia or hypotension
   * start 12.5-25 mg CR/XL, 12.5 mg in class III or IV - then, dose titration every 2 weeks to 50 mg, 100 mg, 200 mg was the target dose. 64% got to target dose, increase dose over 2 months
   * rational: XL formulation gives more accurate 24 hour control, lower peak surges

©PharmReach.org