Erythropoietin May Improve HF-Related Anemia

BY BRUCE JANCIN

BARCELONA — Erythropoietin therapy in patients with anemia of heart failure resulted in improved exercise capacity, reduced heart failure symptoms, and decreased hospitalizations, and showed strong trends for reduced rates of MI and all-cause mortality in a meta-analysis of 11 small randomized clinical trials.

Moreover, erythropoietin was not associated with an increased rate of adverse events, as in some clinical trials carried out in the settings of cancer or chronic kidney disease. It may be that erythropoietin's angiogenesis-promoting effect is therapeutic in the context of heart failure but is the source of side effects in patients with cancer or renal disease, Dr. Dipak Kotecha said at the annual congress of the European Society of Cardiology.

He was quick to offer a caveat, however: "This is all based on a relatively small sample size. Some of these trials were small proof-of-concept trials, others were mechanistic and looked at the effects of different doses. None were individually powered for clinical events. The follow-up was relatively short, at 2-12 months."

The 11 randomized trials involved 794 patients with mild to moderate anemia and left ventricular systolic heart failure. Nine of the trials were placebo controlled. Mean baseline hemoglobin was 10.1-11.8 g/dL and rose by 2.0 g/dL in response to erythropoietin therapy.

This 2.0-g/dL increase in hemoglobin was associated with a mean 69-meter improvement in 6-minute walk distance compared with controls, a 96-second increase in exercise duration, and an improvement in New York Heart Association functional class equivalent to three-quarters of a class.

"All of these changes were clinically as well as statistically highly significant," observed Dr. Kotecha of Royal Brompton Hospital, London.

Peak oxygen consumption, or VO_2 max, increased by an average of 2.3 mL/kg per min. Left ventricular ejection fraction increased in erythropoietin-treated patients by an absolute 5.8% compared with controls; that is comparable to the improvement seen in the major clinical trials of beta-blockers. Quality of life scores using the standard Minnesota and Kansas City instruments showed significant gains as well.

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DR. KOTECHA

Heart failure hospitalizations in erythropoietin-treated patients were significantly reduced by 36% compared with controls, reflecting an absolute 8% rate difference. "The absolute 8% decrease in hospitalizations for heart failure is very similar to what's been seen in the major clinical trials of beta-blocker therapy in heart failure," Dr. Kotecha said.

B-type natriuretic peptide levels fell by an average of 40%, or 237 pg/dL, in response to erythropoietin. Again, that is a magnitude of effect similar to what has been seen in clinical trials of combined beta-blocker and ACE inhibitor or angiotensin receptor blocker therapy, he continued.

The risk of all-cause mortality was reduced by 39% in the erythropoietin treatment group, a strong trend that just missed statistical significance. The 27% relative risk reduction in acute MI also was not quite significant. Definitive answers as to whether erythropoietin therapy has a beneficial effect on these key outcomes are anticipated from the ongoing Amgen-sponsored phase III Reduction of Events With Darbepoetin Alfa in Heart Failure (RED-HF) trial, which is randomizing more than 3,000 patients.

Dr. Kotecha reported having no financial conflicts of interest in connection with the meta-analysis, which was conducted using Cochrane Collaboration methodology and has been submitted to the Cochrane Review for possible publication. ■