# Candesartan Tx Triples Hyperkalemia Risk in HF

BY BRUCE JANCIN
*Denver Bureau*

ATLANTA — Candesartan therapy triples the already significant background risk of potentially serious hyperkalemia in patients with heart failure, according to a new secondary analysis of the Candesartan in Heart Failure—Assessment of Reduction in Mortality and Morbidity (CHARM) program.

Periodic monitoring of serum potassium is therefore "critical" in heart failure patients—and not just those on candesartan, Dr. Akshay Desai said at the annual meeting of the American College of Cardiology.

"The estimate from our study would be that one would expect roughly 34 excess hyperkalemic events per 1,000 candesartan-treated patients over 3 years. However, with careful surveillance of serum potassium this risk can be substantially reduced. In the trial, seven excess serious events per 1,000 patients were noted over the 3-year duration of follow-up with careful monitoring by study investigators. We feel that this represents the unavoidable risk of candesartan therapy in this population of patients," said Dr. Desai of Brigham and Women's Hospital, Boston.

To place this risk in perspective, candesartan also prevented 43 cardiovascular death or hospitalization events per 1,000 patients, the cardiologist added.

The CHARM program involved 7,599 heart failure patients on standard therapy who were randomized in double-blind fashion to candesartan or placebo and followed for just over 3 years with regular monitoring of serum potassium. Candesartan resulted in a significant 16% reduction in the relative risk of the primary end point of cardiovascular death or heart failure hospitalization.

Hyperkalemia is well recognized to be a common and potentially life-threatening complication of treatment with renin-angiotensin-aldosterone system inhibitors. CHARM investigators categorized hyperkalemic events as "serious" if they posed a risk of death or hospitalization, and "concerning" if events were serious or would have become so if not detected early through the monitoring program, with subsequent dose adjustment or drug discontinuation.

The incidence of concerning hyperkalemia during the study was 1.8% in the placebo arm and 5.2% in the candesartan group. Serious hyperkalemic events occurred in 1.1% of the placebo group and 1.8% on candesartan. Of particular clinical relevance was the finding that hyperkalemic events were not confined to the period of candesartan dose titration; they occurred throughout follow-up, although the incidence was greater during titration, Dr. Desai continued.

Several predictors of increased background risk of concerning hyperkalemia were identified. Age greater than 75 years, being on an ACE inhibitor or spironolactone, or a history of diabetes was associated with roughly a twofold increased risk. Baseline renal insufficiency or hyperkalemia conferred a fivefold spike in risk. Candesartan therapy was associated with a threefold increase in risk of hyperkalemia, compared with placebo—but the drug's therapeutic benefit was also consistent across all patient subgroups, including those at high baseline risk for hyperkalemia.

Audience member Dr. Gary S. Francis, director of the coronary intensive care unit at the Cleveland Clinic Foundation, called the new CHARM results "very important data that have practical implications." And he posed a question: "How often should we be monitoring potassium? Because the guideline committees don't have a clue about how to do this."

Dr. Desai replied that the monitoring program used in CHARM, while quite effective in preventing serious events, is probably not readily transferrable to a less motivated real-world population.

"What I would suggest is that, particularly in patients at high baseline risk, be quite careful to measure serum potassium within a 2- to 3-week period after every dose titration, and again intermittently—even randomly—over the course of follow-up to be certain we're not doing our patients harm. Exactly what that interval should be is, I think, an open question," he said. ■

# *Four JCAHO Measures Prove Vital to Heart Failure Outcomes*

BY MITCHEL L. ZOLER
*Philadelphia Bureau*

MADRID — The four criteria now used to measure hospitals' performance in treating patients with heart failure also have a significant impact on patient survival, based on a review of more than 2,000 patients.

In 2002, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) set four core measures for assessing the quality of heart failure management. "To our knowledge, this is the first report showing that adherence to the JCAHO heart failure core measures improves 1-year survival following hospitalization for heart failure," Dr. A.G. Kfoury said at the annual meeting of the International Society for Heart and Lung Transplantation.

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"The data show that these four cheap interventions can have an impact on patient outcomes," said Dr. Kfoury, medical director of the Utah Transplantation Affiliated Hospitals cardiac transplant program, and associate director of the heart failure prevention and treatment program at LDS Hospital in Salt Lake City.

The four performance measures are: discharge instructions to patients on heart failure management, including medications, diet, and weight control; assessment of left ventricular function or scheduling an assessment at discharge; treatment with an ACE inhibitor or angiotensin receptor blocker (ARB) at discharge; and instructions on smoking cessation at discharge.

To determine how the application of these four measures correlated with patient survival, Dr. Kfoury and his associates reviewed the records of 2,144 patients who were discharged with a primary diagnosis of heart failure and left ventricular dysfunction from 20 hospitals within the Intermountain Healthcare system from January 2003 to May 2005. The primary end point of the analysis was death during the 12 months following hospital discharge.

Because 90% of the patients were nonsmokers, one analysis excluded the smoking cessation measure and focused on the application of the other three criteria.

About 43% of patients received all three interventions, and another 39% received two of the interventions. Some 3% of patients received none of the interventions. When only one intervention was used, it was most often prescription of an ACE inhibitor or ARB. The second-most-commonly used intervention was assessment of left ventricular function. Patient education was applied less often.

According to an analysis that adjusted for patients' age, gender, and severity of illness, patients who received none of these three interventions had about a 25% mortality rate during the 12 months following hospital discharge. Patients who received one or two interventions had about a 15% mortality rate, and those who received three interventions had a 10% mortality rate.

When differences between these subgroups were analyzed statistically, patients who received two or three of the JCAHO-prescribed interventions had a significantly improved 12-month survival, compared with the patients who did not, Dr. Kfoury said.

A second analysis looked at the impact of all four interventions, including counseling on smoking cessation. The pattern was quite similar to the prior analysis: Patients who received all four interventions at discharge had a 5% mortality rate over the next 12 months. Those who received none of the interventions had a 25% mortality rate.

"These results should be an impetus to implement these simple but effective measures," said Dr. Kfoury. "Most patients get one or more of the interventions, but patients do not always get all of them." ■

# Depression Post MI Elevates Short-Term, but Not Long-Term Mortality

BY BRUCE JANCIN
*Denver Bureau*

ATLANTA — Depression after MI is associated with markedly increased mortality risk in the first several months following the coronary event, but not increased long-term mortality, Dr. Kapil Parakh said at the annual meeting of the American College of Cardiology.

In a previous report, he and his coinvestigators at Johns Hopkins University, Baltimore, prospectively followed 285 patients with MI who survived to hospital discharge. They determined that patients with at least mild to moderate depression, as evidenced by a Beck Depression Inventory score of 10 or more during hospitalization, had up to a fourfold increased relative risk of mortality at 4 months (Am. J. Cardiol. 2001;88:337-41).

Now Dr. Parakh and coworkers have looked at the same cohort at 3, 5, and 8 years post MI. They found that depression at baseline was not associated with increased mortality at any of these time points.

That depression is common in the first several days post MI and is associated with sharply increased overall mortality in the next several months has been well established in multiple studies.

In contrast, there have been far fewer studies looking at post-MI depression and long-term mortality. Three prior studies have reported increased long-term risk. However, the Hopkins cohort was older, sicker, and more representative of real-world coronary heart disease populations, with several-fold higher prevalences of hypertension and diabetes than in the other studies. The 49% mortality at 8 years in the Hopkins cohort was substantially higher, too. All this may account for the conflicting findings, Dr. Parakh said.

He offered two potential explanations for the lack of increased long-term mortality in the Hopkins patients with depression shortly after MI. One is that patients most vulnerable to the effects of depression got eliminated from the study population because they died early on.

The other possibility is that in a high-risk coronary heart disease population with multiple comorbidities, the association between any single risk factor—such as depression—and outcomes is diminished due to competing comorbidities.

"We've shown in previous work that patients with depression don't follow physician advice to modify their risk, so it may be especially important to look carefully at these patients to help them reduce their risk of events," he said. ■