The benefits were consistent across 20 prespecified subgroups analyzed in the New York Heart Association (NYHA) class II cohort of 2,737 patients. “We believe that the robustness of these findings, in conjunction with the consistent results from the earlier RALES and TOPCAT trials, provides compelling evidence to change medical practice,” said Dr. Zannad, a cardiologist and professor of therapeutics at Henri Poincaré University of Nancy (France).

Current guidelines recommend the use of aldosterone antagonists in moderate to severe heart failure (NYHA class III and IV) and in patients with acute myocardial infarction complicated by left ventricular dysfunction and heart failure. The Randomized Aldactone Evaluation Study (RALES) demonstrated a survival advantage with aldosterone antagonist spironolactone (Aldactone) plus standard therapy in moderate to severe heart failure patients, while the Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study (EPHESUS) did so in the post–MI/heart failure setting.

“The current findings have the potential to greatly expand the use of aldosterone antagonists, which are now utilized by fewer than two-thirds of patients with heart failure in the United States with a current indication.”

“We have three trials in three distinct groups of heart failure severity which essentially have shown the same results,” Dr. Zannad said in an interview. “This puts this class of drugs on equal ground and if anything, the benefit comes on top of the benefit of angiotensin-converting enzyme inhibitors and beta-blockers.”

“Bottom line, he said, is that all patients with a low ejection fraction, provided they have a normal estimated glomerular filtration rate above 30, should be on the three drugs now.” At a press briefing on the study, Dr. Clyde Yancy, immediate past president of the AHA, said that he was enthusiastic about the potential for these drugs to include patients with mild heart failure but that his enthusiasm is tempered by the risk of hyperkalemia. Aldosterone antagonists are known to change the sodium/potassium balance in patients with heart failure by increasing potassium levels. Raising the potassium to within the normal level benefits patients by reducing arrhythmias, but once potassium levels exceed the normal threshold of 5.5 mmol/L, raising potassium levels can independently promote arrhythmias and death.

“You need to always watch for the presence of hyperkalemia with these drugs, but having said that, the benefit is not modest,” Dr. Yancy said. “This is a very real benefit. And again, two-thirds of patients with an indication are not getting these drugs, and that is what I hope will change.”

Hyperkalemia was reported in 8% of patients treated with eplerenone, compared with 3.7% given placebo, Dr. Zannad said. Treatment discontinuation due to hyperkalemia was reported in 1.1% of eplerenone patients and 0.9% of placebo patients, with hospitalization due to hyperkalemia occurring in 0.3% and 0.2% of patients.

In 171 of the 1,364 patients randomized to eplerenone and 213 of the 1,373 patients in the placebo group died. Of these, 147 deaths in the eplerenone group and 185 in the placebo group were due to cardiovascular causes.

Invited discussant Dr. Lynne Warner Stephenson, director of the heart failure program at Brigham and Women’s Hospital in Boston, said that EMPHASIS-HF bridges an “awkward gap in our evidence.”

Major Finding: Eplerenone reduced the risk of cardiovascular death or heart failure hospitalization by 37%, compared with placebo.

Data Source: EMPHASIS-HF, a phase III randomized trial in 2,737 patients with NYHA class II heart failure.

Disclosures: EMPHASIS-HF was funded by Pfizer. Dr. Zannad reported receiving grants from and consulting for Pfizer. Two coauthors are Pfizer employees, and several others reported Pfizer grants and consultancy.

CRT Plus ICD May Reduce Mortality in Mild Heart Failure

The data are likely to change clinical practice, said invited discussant Dr. Clyde W. Yancy, medical director of Baylor Heart and Vascular Institute at Baylor University Medical Center in Dallas and immediate past president of the AHA. He observed that a suite of randomized trials, including COMPANION, CARE-HF, MA-DIT-CRT, reverse, and now RAFT demonstrate compellingly that CRT is effective in heart failure.

“Patients benefit from CRT and we can now extend to patients that have mild heart failure,” he said.

In the pivotal Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy (MADIT-CRT) trial, the use of CRT-ICD therapy decreased the risk of heart failure events but not the risk of death among NYHA class I or II patients with an ejection fraction of 30% or less and a QRS duration of at least 200 milliseconds. CRT with or without an ICD is currently indicated only for the treatment of patients with NYHA functional class III or ambulatory class IV heart failure.

The addition of CRT to an IC significantly reduced the risk of death and heart failure hospitalization by 25% in patients with NYHA class II or III heart failure.

Data Source: Randomized trial in 1,798 patients with mild to moderate heart failure.

Disclosures: RAFT was funded by the Canadian Institutes of Health Research and Medtronic of Canada. Dr. Tang disclosed research support from Medtronic, St. Jude Medical, and Boston Scientific. Dr. Yancy said he had no financial conflicts of interest.

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