

## EDITOR'S PAGE



# The Year in Heart Failure Review 2015 to 2016



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Over the past 12 months, we have seen one of the most exciting times for therapeutic advantages for the patients we serve with congestive heart failure.

We had the approval of 3 therapies that reduced heart failure events; this type of approval success in 1 year is unprecedented.

1. The approval of Sacubitril-Valsartan in heart failure with reduced ejection fraction (HFrEF) for the reduction in mortality and heart failure hospitalizations plus mortality.
2. Ivabradine in HFrEF for the reduction in heart failure hospitalizations.
3. Pulmonary artery pressure monitor for patients with class 3 heart failure to reduce heart failure admissions.

We also learned of an important number of neutral and negative trials that have benefited our patients. We discovered that adaptive servo-ventilation, positive airway pressure therapy, in central sleep apnea patients with HFrEF demonstrated an increase in mortality and cardiovascular mortality, and had no advantage on the composite endpoints of heart failure hospitalization, death, or other secondary endpoints, such as quality of life. These results brought into question the use of adaptive servo-ventilation in patients with central sleep apnea, and therefore, the strategy was removed from the international community. This therapy was not used frequently in the United States, but was used frequently in Japan and parts of Europe.

We had 2 significant Heart Failure Network phase 2 studies that had negative results:

1. The unique trial of isosorbide mononitrate in patients with HFpEF, which was a randomized, double-blind, placebo-controlled, crossover study of nitrate therapy versus placebo. The primary

endpoint of physical activity was measured by the average daily accelerometer units. In this study, nitrates proved to be inferior in increasing activity in HFpEF patients. It demonstrated less hours of activity per day with more side effects in the population of HFpEF patients in which this drug has been used, in up to 25% of patients with HFpEF.

2. A Phase 2 study consisted of liraglutide for high-risk patients with HFrEF in the FIGHT study. In this study, patients were randomized at the time of discharge from the hospitalization to drug therapy versus placebo. The study looked at the global endpoint rank of change in N-terminal pro-B-type natriuretic peptide, HF hospitalization, or death and found no significant difference. However, there were trends toward worse outcomes in the liraglutide group, in which death or heart failure hospitalization (up to 180 days) had a hazard ratio of 1.3, and although not significant, this was troublesome as were other side effects of the drug.

This year we also presented the National Heart, Lung, and Blood Institute-funded SPRINT trial, which was a strategy trial of reducing blood pressure to <120 mm Hg in the intensive therapy line versus 140 mm Hg in the usual care group. This trial showed a significant reduction in heart failure events and mortality.

Two promising phase 2 studies of vericiguat, a soluble guanylate cyclase activator that improves surrogate endpoints in HFrEF and HFpEF patients, and omecamtiv mecarbil showed improved surrogate endpoints in chronic HFrEF patients.

The new type 2 diabetes drug empagliflozin, a selective inhibitor of sodium-glucose cotransporter 2, was studied in high-risk patients with type 2 diabetes in the EMPA-REG Outcome Trial.

This study included 7,020 patients, and demonstrated empagliflozin reduced the risk of the primary composite endpoint of cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke, as well as the hospitalization rate for heart failure.

Thus, the past year was an impressive one for heart failure advances. Clinical trials continue to improve the way we take care of patients, regardless of whether they are positive or negative. Let us continue

to commit ourselves to the pursuit of knowledge and the participation in randomized controlled clinical trials.

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