

## Letters to the Editor

### Reply to Letter From Floras et al.—Central Sleep Apnea: Risk Factor or Pathogenic Process in Patients With Heart Failure



#### To the Editor:

We thank Floras et al.<sup>1</sup> for their interest in our News and Commentary on the use of adaptive servo-ventilation (ASV) therapy in symptomatic patients with heart failure and reduced ejection fraction.<sup>2</sup> As clearly delineated in our News and Commentary, the safety advisory was issued based on the findings of increased mortality in patients receiving ASV in the Adaptive Servo-Ventilation for Central Sleep Apnea in Systolic Heart Failure (SERVE-HF) trial. The actual results of the trial were presented at the 2015 European Society of Cardiology Congress and recently published in the *New England Journal of Medicine*.<sup>3</sup>

The trial conformed to the high standards we have come to expect from large multicentre randomized clinical trials, including the primary analysis on adjudicated end points in the intention-to-treat population, which would account for nonadherence in the trial. The published study clearly demonstrated increased overall mortality (hazard ratio, 1.28;  $P = 0.01$ ) and cardiovascular mortality (hazard ratio, 1.34;  $P = 0.006$ ), findings that triggered the release of the field safety notice calling for the termination of ASV therapy as routine therapy for central sleep apnea (CSA) in patients with heart failure with reduced ejection fraction outside the clinical trial setting. The 15% crossover from the control therapy arm to positive airway pressure therapy was dominated by the use of ASV (90%), whereas a larger percentage of patients in the ASV arm (26%) discontinued therapy, which would instead minimize the adverse effects seen with ASV therapy.

As we argued in our News and Commentary, CSA may indeed represent a *risk factor* or compensatory mechanism rather than a *pathogenic* process in heart failure, a finding supported by the results of the SERVE-HF trial, in which patients with a greater proportion of Cheyne-Stokes respiration had increased risk of all-cause death or lifesaving cardiovascular intervention plus unplanned hospitalization for

worsening chronic heart failure ( $P = 0.006$ ).<sup>3</sup> The use of ASV is further complicated by the recent findings that the use of ASV for 24 weeks in patients with heart failure and reduced ejection fraction resulted in an improved quality of life measure—a subjective measure—while leaving objective measures of heart failure prognosis, plasma brain natriuretic peptide, and left ventricular ejection fraction unchanged.<sup>4</sup>

Given the notable differences from the SERVE-HF trial,<sup>1</sup> we eagerly await the results of the Effect of Adaptive Servo Ventilation (ASV) on Survival and Hospital Admissions in Heart Failure (ADVENT-HF) trial to further define the use and safety of ASV therapy in patients with heart failure and reduced ejection fraction. We applaud Floras et al. for highlighting the close monitoring of the ADVENT-HF trial by the data Safety and Management Committee,<sup>1</sup> a position we endorsed in our News and Commentary.<sup>2</sup>

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#### Disclosures

The authors have no conflicts of interest to disclose.

#### References

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