ResMed presents data on Phase IV SERVE-HF study of Adaptive Servo-Ventilation therapy in central sleep apnea and chronic symptomatic heart failure at ESC Congress 2015

Study did not meet primary endpoint and adaptive servo-ventilation has no significant benefit in patients with symptomatic chronic heart failure and reduced ejection fraction and predominant central sleep apnea

LONDON – 1st September, 2015 – ResMed (NYSE: RMD) today presented data from the SERVE-HF study at ESC Congress 2015 in London.

SERVE-HF, a multinational, multicenter, randomized controlled Phase IV trial of 1,325 patients, was designed to investigate the effects of adding adaptive servo-ventilation (ASV) therapy to guideline-based medical management on survival and cardiovascular outcomes in patients with symptomatic chronic heart failure (NYHA 2-4) and reduced ejection fraction (LVEF ≤45%) and moderate to severe predominant central sleep apnea (CSA) (AHI > 15/h, ≥ 50% central events, cAHI ≥ 10/h). The primary endpoint of the study was death from any cause ("all-cause mortality"), a life-saving cardiovascular intervention or unplanned hospitalization for worsening chronic heart failure.

Earlier this year, preliminary analysis of the SERVE-HF data resulted in ResMed updating the labelling for its ASV devices, contraindicating the specific group of patients with symptomatic chronic heart failure, reduced ejection fraction (LVEF ≤45%) and predominant CSA that were included in SERVE-HF.

Results Summary

- The study showed that ASV therapy effectively controlled central sleep apnea. Sixty-percent of patients randomized to ASV therapy used it for at least three hours per night.
- Incidence of the primary endpoint did not differ significantly between the ASV and control groups (54.1% versus 50.8%, respectively; hazard ratio [HR] 1.13; 95% confidence interval [CI] 0.97, 1.31; P=0.10).[1] There was significant effect modification for the primary end point by the degree of Cheyne-Stokes respiration.
- All-cause and cardiovascular mortality were significantly higher in the ASV group than in the control group (HR 1.28, 95% CI 1.06, 1.55; P=0.01 and 1.34, 95% CI 1.09, 1.65; P=0.006, respectively, indicating ASV therapy should not be used to treat predominant CSA in patients with symptomatic heart failure and reduced ejection fraction (LVEF ≤45%).[2] The effect on cardiovascular mortality was significantly modified by the degree of left ventricular impairment. There were no adverse events during the SERVE-HF study associated with the performance of the ASV therapy device.

Professor Martin R Cowie, Professor of Cardiology at Imperial College London (Royal Brompton Hospital), co-principal investigator of the study said: "SERVE-HF is a high-quality, landmark trial in the study of patients with symptomatic heart failure and reduced ejection fraction who also have CSA. The results showed that despite reasonable adherence to ASV and effective control of CSA by ASV, the results for the primary endpoint were neutral, with no significant difference between patients treated with ASV and the control group."

"The fact that ASV therapy increased the risk of death in this specific patient population is an unexpected, but clinically highly important, finding. Further research will need to be conducted and precautions taken but the hope is that these findings will make the management of this frail patient population safer."

Holger Woehrle, VP Clinical Research and Medical Director of ResMed Europe and Asia Pacific, said: "As a pioneer in high quality research in this field, ResMed remains committed to studying how managing sleep-disordered breathing may help people with cardiovascular conditions, from hypertension and coronary artery disease to atrial fibrillation, heart failure and stroke."

"While this was an unexpected result, the findings remain vitally important for the heart failure community and for patients with chronic heart failure, reduced ejection fraction and predominant central sleep apnea. It is important that we do not extrapolate these findings beyond the specific population and parameters that were investigated in SERVE-HF. The results cannot, and should not, be applied to people with CSA in the absence of systolic heart failure, or to people with obstructive sleep apnea (OSA) with or without chronic symptomatic heart failure.The trial results also do not apply to continuous / automatic positive airway pressure devices (CPAP or APAP), which continue to play a vital role in treating OSA for millions of people."

Analysis of the data from the SERVE-HF sub-study is ongoing. ResMed will continue to publish updates via http://serve-hffaqs.com for healthcare providers and patients who have questions or would like more information.

Notes to Editors

About Sleep-Disordered Breathing (SDB)

SDB encompasses a spectrum of breathing problems during sleep, including repetitive pauses in breathing during sleep. The two most common types of SDB are obstructive sleep apnea (OSA) and central sleep apnea (CSA).

OSA is a disorder in which the throat muscles relax, block the airways and stop the flow of breath during sleep.

CSA is a disorder in which the brain does not transmit the “breathe” signal to the muscles that control breathing during sleep. In some cases, people with CSA also exhibit an abnormal breathing pattern known as Cheyne-Stokes respiration. With Cheyne-Stokes respiration, there is a period of shallow breathing followed by deep breathing, with intermittent central apnea, in which the breath is stopped for more than 10 seconds during each apnea.

CSA with Cheyne-Stokes respiration (CSA-CSR) is rare in the general population but is quite common in patients with symptomatic chronic HF, at a rate of 20-45%.[3]

About Adaptive Servo-Ventilation (ASV) therapy

ASV refers to a therapy specifically designed to treat CSA-CSR, in which a patient’s ventilation is monitored and stabilized through adaptive positive airway pressure, supplied via a mask worn by the patient.

About ResMed

The global team at ResMed (NYSE:RMD) is united in the commitment to change millions of lives with every breath. With more than 4,000 employees and a presence in over 100 countries, the company has been pioneering new and innovative devices and treatments for sleep-disordered breathing, chronic obstructive pulmonary disease, and other chronic diseases for more than 25 years. ResMed's world-leading products and innovative solutions improve quality of life for millions of patients worldwide, reduce the impact of chronic disease, and save healthcare costs. For more information about ResMed and its business, visit www.resmed.com or follow @resmed on Twitter.

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