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New results from the SHIFT study in heart failure patients with Corlentor[®]: for the first time, direct link found between reducing heart rate and quality of life

Madrid, Spain, 1 September 2011 -- New results from SHIFT (Systolic Heart Failure Treatment with the I_f Inhibitor Ivabradine Trial), the largest-ever morbi-mortality study of treatments for chronic heart failure, reveal for the first time a direct link between heart rate reduction and quality of life in patients with heart failure.ⁱ

The new data from the SHIFT study with Corlentor[®] (ivabradine), presented today at the European Society of Cardiology congress, are clinically important as quality of life is greatly impaired in patients with chronic heart failure and poor quality of life in these patients is associated with worse disease outcomes.

"The main SHIFT results presented at last year's ESC congress clearly told us that the I_f Inhibitor Corlentor[®] prevents the progression of heart failure and improves survival", explained SHIFT study co-chairman Prof Karl Swedberg, University of Gothenburg, Sweden. "Our new analyses show that Corlentor[®] also improves the quality of life as reported by patients with heart failure and that this improvement is directly proportional to heart rate reduction. Put simply, we found that, the lower the heart rate, the better the quality of life and the better the patient outcome."

The new SHIFT analysis set out to assess if quality of life in heart failure patients was related to prognosis and changes in heart rate. It involved 1944 patients with chronic heart failure from 24 countries who were randomised to receive either Corlentor[®] or placebo on top of standard heart failure therapy. Health related quality of life was assessed using the Kansas City Cardiomyopathy Questionnaire (KCCQ), a validated,

disease-specific measure of functional status and quality of life.ⁱⁱ The 23 items of the questionnaire are divided into 2 sets of scores, the clinical summary score assessing physical limitation and symptoms and the overall summary score assessing social limitation in chronic heart failure patients. The higher the score, the better the quality of life.

By one year, the study showed that the risk of a cardiovascular event increased in patients with lower KCCQ scores (equating to a lower health related QoL). The reduction in heart rate achieved through treatment with Corlentor[®] was associated with almost double the improvement in quality of life compared to the control group. This improvement was observed in both the disease related component and the social component of the scores. Practically speaking, this means that patients who received Corlentor[®] were able to participate in a greater number of everyday activities, considerably changing their day to day life. Thus, with these new results it is important to note that heart rate reduction with Corlentor[®], unlike beta-blockers, improves both survival and QOL in heart failure patients.

SHIFT findings explained by new echocardiography data

An additional sub-study from SHIFT, also presented today at the ESC congress, provides insight into why Corlentor[®] achieves improvements in the symptoms, prognosis, quality of life and survival rates in heart failure patients.

The SHIFT echocardiography study was carried out in 411 patients. Echocardiograms were performed at baseline and after eight months of Corlentor[®] treatment or placebo. The study showed that Corlentor[®] significantly reduced left ventricular volumes and improved left ventricular ejection fraction.ⁱⁱⁱ

Left ventricular end-systolic volume -- the amount of blood in the left ventricle at the end of contraction -- is a well-recognised prognostic factor and increased end-systolic volume is a sign that the heart is not pumping effectively.

"Our echocardiography study shows that Corlentor[®] significantly reduces the size of the left ventricle and improves the remodeling and pumping function of the heart",

says Professor Jean-Claude Tardif from the Montreal Heart Institute at the University of Montreal in Canada.

The results from these sub-studies complement the main findings of the SHIFT study which showed that Corlentor[®] reduced the risk of hospitalisation due to worsening heart failure by over a quarter (26%, $p < 0.0001$) and the likelihood of death from heart failure by the same amount (26%, $p = 0.014$). Despite the fact that patients were already well treated, these benefits were seen in just three months of treatment with Corlentor[®].

Chronic heart failure affects 15 million patients in Europe (2% to 3% of the overall population). It impairs the heart's ability to pump effectively and maintain sufficient circulation to meet the body's needs.

"The objectives of treating heart failure are to improve symptoms, quality of life, improve prognosis and prevent disease progression. The SHIFT study and all the new analyses demonstrate that Corlentor[®] achieves these objectives over and above the best possible recommended therapy", concludes Professor Michel Komajda, co-chairman of the SHIFT Executive Committee from Pierre and Marie Curie Paris 6 University, France.

Corlentor[®] is currently indicated for the treatment of the symptoms of chronic chest angina in adults with coronary disease and a normal sinus rhythm, who are intolerant to beta-blockers or contraindicated for them, or in association with betablockers, in patients where the disease is not controlled adequately by an optimal dosage of betablockers, and who have a heart rate of above 60 beats per minute. Corlentor[®] (ivabradine) is a product that has been developed by *Les Laboratoires Servier* and is marketed by them as Procolaran[®].

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ⁱ Ekman I et al. Heart rate reduction with ivabradine and health related quality of life in patients with chronic heart failure Results from SHIFT. *European Heart Journal*, Published Online 29th August 2011

ⁱⁱ Green CP, Porter CB, Bresnahan DR, Spertus JA. Development and evaluation of the Kansas City Cardiomyopathy Questionnaire: a new health status measure for heart failure. *J. Am. Coll. Cardiol.* 2000;35;1245-1255

ⁱⁱⁱ Tardif J-C et al. Effects of selective heart rate reduction with ivabradine on left ventricular remodeling and function: results from the SHIFT echocardiography substudy. *European Heart Journal*, Published Online 29th August 2011