

Rationale and design of a multicentre, randomized, placebo-controlled trial of mirabegron, a Beta₃-adrenergic receptor agonist on left ventricular mass and diastolic function in patients with structural heart disease Beta₃-left ventricular hypertrophy (Beta₃-LVH)

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Abstract

Aims

Progressive left ventricular (LV) remodelling with cardiac myocyte hypertrophy, myocardial fibrosis, and endothelial dysfunction plays a key role in the onset and progression of heart failure with preserved ejection fraction. The Beta₃-LVH trial will test the hypothesis that the β₃ adrenergic receptor agonist mirabegron will improve LV hypertrophy and diastolic function in patients with hypertensive structural heart disease at high risk for developing heart failure with preserved ejection fraction.

Methods and results

Beta₃-LVH is a randomized, placebo-controlled, double-blind, two-armed, multicentre, European, parallel group study. A total of 296 patients will be randomly assigned to receive either mirabegron 50 mg daily or placebo over 12 months. The main inclusion criterion is the presence of LV hypertrophy, that is, increased LV mass index (LVMI) or increased wall thickening by echocardiography. The co-primary endpoints are a change in LVMI by cardiac magnetic resonance imaging and a change in LV diastolic function (assessed by the E/e' ratio). Secondary endpoints include mirabegron's effects on cardiac fibrosis, left atrial volume index, maximal exercise capacity, and laboratory markers. Two substudies will evaluate mirabegron's effect on endothelial function by pulse amplitude tonometry and brown fat activity by positron emission tomography using 17F-fluorodeoxyglucose. Morbidity and mortality as well as safety aspects will also be assessed.

Conclusions

Beta3-LVH is the first large-scale clinical trial to evaluate the effects of mirabegron on LVMI and diastolic function in patients with LVH. Beta3-LVH will provide important information about the clinical course of this condition and may have significant impact on treatment strategies and future trials in these patients.

Keywords

β 3 adrenergic receptor Mirabegron Hypertensive structural heart disease Heart failure with preserved ejection fraction