Antihypertensive Efficacy of LCZ696 (Sacubitril/Valsartan) in Hypertension

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Essential hypertension is a complex clinical condition, characterized by sustained elevation of systolic and/or diastolic blood pressure (BP) levels and an increased risk of developing major cardiovascular (CV) outcomes, mostly including coronary artery disease, stroke, and death. Several studies have also reported that high BP levels are significantly related to a higher risk of new-onset congestive heart failure than normotension and that hypertensive disease (i.e., left ventricular diastolic dysfunction with or without left ventricular remodeling or hypertrophy) may be responsible of the progression from hypertension toward left ventricular systolic dysfunction and clinically evident heart failure, independently of the presence of concomitant conditions and comorbidities [1].

Current guidelines for the clinical management of heart failure have highlighted the progressive nature of the disease, which is summarized by the concept of a “cardiovascular continuum” [2]. This is the reason why preventive strategies aimed at reducing the risk of developing heart failure are currently based on the use of different classes of antihypertensive agents, mostly including drugs inhibiting the renin-angiotensin-aldosterone system, such as angiotensin-converting enzyme inhibitors,

angiotensin receptor blockers (ARB), and antialdosterone agents [3–5].

Over the last few years, several new drug classes have been developed and tested for the clinical management of hypertension and, thus, for the prevention of hypertension-related CV diseases, including heart failure. While some classes have shown negative results, some others classes seem to provide favorable results. Among these classes, drug therapy based on LCZ696 (sacubitril/valsartan), a first-in-class angiotensin receptor-neprilysin inhibitor, at different dosages has been demonstrated to improve CV morbidity and mortality in high-risk patients with heart failure [6, 7].

It should be noted, however, that LCZ696 was originally developed for the clinical management of hypertension and that the use of this drug has been shown to provide marked BP reductions both in systolic and in diastolic BP levels [8]. This might have a clinical impact on heart failure patients, since the beneficial effects provided by this drug at both cardiac and vascular levels might be counterbalanced by excessive BP reductions, a reduced cardiac output, hypotension, and fatigue [9].

The article by Hou et al. [10] is a meta-analysis of 12 clinical studies and a total of 6,064 patients, aimed at eval-

uating the antihypertensive efficacy of LCZ696. Compared with ARB, LCZ696 demonstrated greater reductions in both clinical and 24-h ambulatory systolic/diastolic BP levels. The BP-lowering effect was consistently observed across different clinical studies and was found to be dose-dependent and largely independent of age and baseline BP values, which ranged within stage 1–2 hypertension. These results confirmed and extended those of previous analyses, which showed similar beneficial effects on BP reduction [11].

Based on the available evidence, the BP reductions produced by the use of angiotensin receptor-neprilysin inhibitor can be effectively and safely used for the clinical management of high BP in heart failure patients (albeit outside of the approved indication). On the other hand,

this therapeutic effect should be always kept in mind when treating heart failure patients with low BP levels at baseline.

Conflict of Interest Statement

G.T. has no conflict of interests to disclose.

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Author Contributions

G.T. conceived, prepared, and revised this paper in its present form.

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