PARAMETER Study: LCZ696 Safe and Effective in Reducing Systolic and Pulse Pressure

Written by Alla Zarifyan

Bryan Williams, MD, University College London, London, United Kingdom, presented principal results of the PARAMETER study demonstrating that in older patients with systolic hypertension and arterial stiffness, the angiotensin receptor neprilysin inhibitor LCZ696 reduced central aortic systolic pressure (CASP) and central pulse pressure (CPP) more effectively than olmesartan, an angiotensin receptor blocker.

Hypertension in elderly patients is characterized by elevated systolic blood pressure (SBP) and increased CPP, which indicate large artery aging and stiffness and are predictive of cardiovascular disease and heart failure.

PARAMETER was a multicenter, randomized, double-blind, active-controlled, 52-week study designed to evaluate the safety and efficacy of LCZ696 on CASP and arterial stiffness in elderly patients with hypertension [Williams B et al. *BMJ Open*. 2014]. The patients were aged ≥60 years, with a SBP ≥150 mm Hg and pulse pressure (PP) >60 mm Hg.

A total of 454 patients were enrolled and randomized to LCZ696 200 mg daily (n=229) or olmesartan 20 mg daily (n=225) for 4 weeks, followed by a forced titration to double the initial doses for the next 8 weeks. The primary and the key secondary end points were evaluated at 12 weeks to determine the effect of LCZ696 400 mg daily vs olmesartan 40 mg daily on reducing CASP and CPP, respectively. Thereafter, patients with uncontrolled BP received add-on therapy as needed. Patients were followed for an additional 40 weeks after the initial evaluation, for a total follow-up period of 52 weeks.

At 12 weeks, the reduction in CASP was significantly higher with LCZ696 compared with olmesartan, at −12.6 mm Hg vs −8.9 mm Hg ($P=.01$). CPP was also reduced more significantly by LCZ696 compared with olmesartan, at −6.4 mm Hg vs −4.0 mm Hg ($P=.012$).

Brachial SBP at 12 weeks was lowered by 13.7 mm Hg vs 9.9 mm Hg with LCZ696 vs olmesartan, respectively ($P=.016$), while PP was lowered by 7.7 mm Hg vs 4.9 mm Hg ($P=.013$), respectively. LCZ696 also significantly lowered 24-hour brachial and central aortic SBP ($P<.001$ for both) compared with olmesartan, with the biggest difference between treatment groups occurring at night.

NT-proBNP, a marker for ventricular-vascular coupling, was lowered by 34% vs 20% with LCZ696 vs olmesartan, respectively.

At 52 weeks, CASP was lowered by 16.2 mm Hg with LCZ696 vs 14.7 mm Hg with olmesartan ($P=.27$), while CPP was lowered by 7.2 mm Hg vs 6.6 mm Hg ($P=.6$), respectively. Brachial SBP was lowered by 17.7 mm Hg vs 16.1 mm Hg with LCZ696 vs olmesartan, respectively ($P=.28$), while brachial PP was lowered by 8.8 mm Hg vs 8.0 mm Hg, respectively ($P=.48$).

Monotherapy was sufficient in 68% of patients treated with LCZ696 vs 53% of those treated with olmesartan. Both LCZ696 and olmesartan treatments were safe and well tolerated, and the key safety parameters (including any adverse events [AEs], serious AEs, or discontinuation due to AEs, serious AEs, drug-related AEs, or death) did not vary significantly between the groups.

Prof Williams summarized that the PARAMETER study met its primary and key secondary objectives and that LCZ696 provided beneficial effects on central aortic hemodynamics and function and can offer a therapeutic advantage beyond those observed with renin–angiotensin system blockade.

Extended DAPT Reduces Secondary Cardiovascular Events in Patients With Prior MI

Written by Alla Zarifyan

A meta-analysis of randomized controlled trials has demonstrated a substantial reduction in cardiovascular (CV) outcomes, including CV mortality, with dual antiplatelet therapy (DAPT) continued beyond 1 year vs aspirin alone, among patients with a prior myocardial infarction (MI) [Udell JA et al. *Eur Heart J*. 2015].

The recent trials examining the effect of extended DAPT in a variety of patient populations have produced heterogeneous results regarding its safety and efficacy, according to Jacob A. Udell, MD, MPH, University of Toronto, Toronto, Canada. He noted that in clinical practice DAPT is stopped at 1 year in about 50% of patients because of the lack of long-term data.

Dr Udell and colleagues conducted a systematic review and meta-analysis that evaluated whether long-term DAPT reduced CV risk when compared with aspirin alone in patients with a history of prior MI. The primary end point was a composite of major adverse CV events (MACEs) defined as CV death, MI, and stroke. The secondary end points included CV death, MI, stroke, non-CV death, all-cause mortality, major bleeding, and stent thrombosis.

The key features of the 6 trials included in the meta-analysis are shown in Table 1. The mean follow-up was 30 months, and there was a total of 2273 MACEs. The mean age of the patients was 64 years; 24% were women; and the mean time from MI was 18 months. Notably, few patients