Journal of the American Society of Hypertension 8(4S) (2014) e27–e34

POSTER SESSION I

ANTIHYPERTENSIVE DRUGS AND PHARMACOLOGY

P-1

A randomized, open-label, blinded-endpoint, active-comparator, forced-titration study to compare nebivolol versus metoprolol as dual therapy with amlodipine in patients with hypertension: results of the tandem study

Henry A. Punzi[1,2] [1]*Punzi Medical Center, Carrollton, TX, United States;* [2]*UT Southwestern Medical Center, Dallas, TX, United States*

We assessed the efficacy of blood pressure control and pedal edema of Nebivolol (N) 10 force titrated to 20 mg once-daily compared to Metoprolol (M) 50 force titrated to 100 mg once daily in patients on baseline Amlodipine (A) 10 mg once daily. Adults with stage 1 or 2 hypertension were randomized, and started a 4-week A monotherapy treatment phase. This was followed by a 4-week low dose N/M treatment phase as add on therapy to A and a subsequent 4-week forced titration to high dose N/M in addition to A therapy. All patients underwent 24 ambulatory blood pressure monitoring (ABPM) as well as measurement of leg edema by EDEMAT (E) at Day -1, week 4, week 8 and week 12. Safety and tolerability were assessed by recording treatment-emergent adverse events (TEAEs), monitoring vital signs and clinical laboratory parameters, and performing ECGs and physical examinations. Of 41 patients, a total of 10 patients in the N arm of the study were aged ≥60 years of age (70% men and 30% women) and a total of 6 patients in the M arm of the study were aged ≥60 years of age (66% men and 33% women) . TEAE were experienced by 94% of patients and were mostly mild or moderate in severity. The most common TEAE in those prescribed A/N were URI (23.5%), bronchitis (9.0%), blurred vision in both eyes intermittently (9.0%), swelling of both ankles (4.5%), swelling of hands (4.5%) and swelling of both feet (4.5%). The most common TEAE prescribed A/M were URI (13.6%), bronchitis (14.6%), intermittent dizziness (5.9%), swelling of both legs and feet (5.9%), and headache (5.9%). There were no syncope or serious AEs experienced and no deaths occurred. In the A/N arm, the mean baseline office BP of patients was 148/97 mmHg, mean baseline ABPM of patients was 148/83mmHg and mean E was 1357.9 gms. After 12 weeks of treatment, mean office BP was 130/78 mmHg (a SBP reduction of 18 mmHg and a DBP reduction of 19 mmHg) and mean ABPM of patients was 121/67mmHg (an ambulatory SBP reduction of 27 and an ambulatory DBP reduction of 16 mmHg) and mean E measurement difference of 133.8gms. In the A/M arm, the mean baseline office BP of patients was 154/97 mmHg, mean baseline ABPM was 149/84mmHg and mean E was 1365.2gms. After 12 weeks of treatment, mean office BP was 131/80 mmHg (a SBP reduction of 23 mmHg and a DBP reduction of 17 mmHg.) and mean ABPM was 125/71 mmHg (an ambulatory SBP reduction of 24 mmHg and an ambulatory DBP reduction of 13 mmHg) and mean E measurement difference of 148.5 gm. In conclusion, A/N treatment had superior ABPM reduction with less edema when compared to A/M. A/N therapy fulfills the JNC 8 guideline recommendation that when achieving SBP < 140 mm Hg in 60 yo it was well tolerated and had less edema improving quality of life and would not need to be adjusted.

Keywords: nebivolol; beta blocker; amlodipine; edema

P-2

Age and the efficacy of LCZ696, an angiotensin receptor-neprilysin inhibitor (ARNI), compared to valsartan in patients with systolic hypertension

Joseph L. Izzo,[†,2] *Dion H. Zappe,*[1] *Yan Jia,*[1] *Kudsia Hafeez,*[1] *Jack Zhang.*[1] [1]*Novartis Pharmaceuticals, East Hanover, NJ, United States;* [2]*University at Buffalo, Buffalo, NY, United States*

Effective control of systolic hypertension (SH) can be difficult to achieve. LCZ696 (Japanese Adopted Name: sucabitril valsartan sodium hydrate) is a first-in-class ARNI that may be uniquely effective in treating SH patients. This 8-week, multicenter, randomized, double-blind, placebo- and active-controlled study in patients with SH (mean sitting [ms] systolic blood pressure [SBP] ≥150 mmHg at baseline) compared the efficacy of LCZ696 to valsartan (V), varying doses of V + neprilysin, and placebo. Within the protocol, 285 of 907 patients (mean age 61 yrs, 68% Caucasian, mean body mass index 29.9 kg/m2) were randomized to V 320 mg (n=143) or LCZ696 400 mg (n=142).

Subjects were then dichotomized by age for this sub-analysis.

Those ≥65 yrs (47.4%) had equivalent baseline msSBP (160.6 vs. 159.0 mmHg) but lower baseline msDBP (86.4 vs. 93.7 mmHg) than those <65; 79 subjects 65 received LCZ696 and V, respectively. Both LCZ696 and V caused substantial reductions in SBP and DBP at week 8 compared to baseline (table, P<0.001 each). LCZ696 400 mg lowered msSBP and msPP to a greater extent than V in those ≥65, while in those <65, LCZ696 lowered msDBP to a greater degree than V (Table). All treatments were well tolerated, with a similar overall incidence of adverse events (25.8% and 23.8% in those aged under and over 65 yrs; 30.2% and 25.7% in those taking LCZ696 and V, respectively).

We conclude that, in patients with SH: (1) LCZ696 is more effective than V in reducing BP; (2) LCZ696 causes greater SBP lowering than V in those age 65 or older but slightly greater DBP lowering in those under 65; and (3) both drugs are safe and well tolerated in a short-term study irrespective of age.

Table
LCZ696 400 mg and valsartan 320 mg daily at week 8

	V (Δ from baseline, mmHg)		LCZ696 (Δ from baseline, mmHg)		Difference between treatments (LCZ696 - V, mmHg)	
		≥65 yrs		≥65 yrs		≥65 yrs
Δ msSBP	-17.0 (1.7)	-15.5 (1.7)	-21.1 (1.6)	-22.8 (1.8)	-4.1(2.3)	-7.35 (2.5)*
Δ msDBP	-6.9 (1.1)	-7.6 (1.0)	-10.25 (1.1)	-8.9 (1.0)	-3.3 (1.6)*	-1.3 (1.4)
Δ msPP	-9.9 (1.1)	-7.9 (1.4)	-10.75 (1.1)	-14.0 (1.5)	-0.9 (1.6)	-6.1 (2.05)*

Least square means ± standard errors (SE); *p<0.05.