expression and MLC-P, implicating ras-regulated myosin phosphorylation in Ang II signaling observed in hypertensive disease.

Key Words: Angiotensin II, Hypertension, Myosin Light Chain Kinase

P-157
ASSOCIATION OF C825T POLYMORPHISM OF THE G PROTEIN β3-SUBUNIT WITH ANTIHYPERTENSIVE RESPONSE TO A THIAZIDE DIURETIC
Qi Hua, Dongbao Li, Lin Pi, Cardiology, Beijing Xuanwu Hospital, Beijing, China; China.

Objective: To investigate the association of T allele of the C825T polymorphism of the gene encoding the β3-subunit of G proteins (GNB3) with blood pressure response to diuretic therapy.

Methods: Polymerase chain reaction combined with restriction enzyme digestion was used to detect the polymorphism of G protein of β3 subunit gene in 147 normotensive controls and 321 hypertensive patients. 48 hypertensive patients underwent monotherapy with hydrochlorothiazide for 4 weeks.

Results: Mean declines in systolic and diastolic blood pressures were significantly greater in CT heterozygotes and TT homozygous (22.67 ± 13.74 mmHg, 12.00 ± 9.39 mmHg) than in CC homozygotes (8.81 ± 6.23 mmHg, 6.50 ± 5.32 mmHg). In multiple regression models, the TT genotype remained a significant predictor of greater declines in systolic and diastolic blood pressures, (p<0.05). There were no significant differences of the GNB3 gene C825T polymorphism genotypes and alleles between hypertensive patients (CC: 28.7%, CT: 52%, TT: 19.3% and C: 50.7%, T: 49.3%) and normotensive controls (CC: 27.2%, CT: 46.9%, TT: 25.9% and C: 50.7%, T: 49.3%).

Conclusions: The C825T polymorphism of GNB3 may help identify patients with essential hypertension who are more responsive to hydrochlorothiazide therapy, but the C825T polymorphism of GNB3 is not associated with essential hypertension.

Key Words: Diuretics, Blood Pressure, Essential Hypertension

P-158
EFFICACY OF OLMESARTAN MEDOXOMIL (O) AND O/HYDROCHLOROTHIAZIDE (H) IN ACHIEVING BLOOD PRESSURE (BP) CONTROL AND NORMALIZATION IN STAGE 2 SYSTOLIC HYPERTENSION (HTN)
Joseph Izzo, Joel Neutel, Robert Dubiel, Findlay Walker, Dept. of Medicine, SUNY at Buffalo, Buffalo, NY; Dir. of Research, Orange County Research Center, Tustin, CA; Medical Affairs, Sankyo Pharma Inc, Parsippany, NJ.

The JNC 7 report stresses the importance of reducing systolic BP (SBP) and states that ≥2 agents are usually required to achieve goal BP (<160 mmHg) in Stage 2 systolic HTN. This study evaluated the efficacy of an open label titration regimen using the angiotensin receptor blocker O alone and in combination with H to achieve goal BP (<140/90 mmHg) and to normalize BP (alone and in combination with H) to achieve goal BP and 27% achieving normal BP. This study evaluated the metabolic consequences and safety of an open label titration regimen of the angiotensin receptor blocker OLM alone and in combination with HCTZ in Stage 2 systolic HTN. After a placebo run-in, patients (pts) (N=169) with seated SBP ≥160 and <200 mmHg and diastolic BP (DBP) <110 mmHg received OLM 20 mg/d for 3 wks.

P-159
METABOLIC EFFECTS AND SAFETY OF HYDROCHLOROTHIAZIDE (HCTZ) IN COMBINATION WITH OLMESARTAN MEDOXOMIL (OLM) IN STAGE 2 SYSTOLIC HYPERTENSION (HTN)
Joseph Izzo, Joel Neutel, Robert Dubiel, Findlay Walker, Dept. of Medicine, SUNY at Buffalo, Buffalo, NY; Dir. of Research, Orange County Research Center, Tustin, CA; Medical Affairs, Sankyo Pharma Inc, Parsippany, NJ.

This study evaluated the metabolic consequences and safety of an open label titration regimen of the angiotensin receptor blocker OLM alone and in combination with HCTZ in Stage 2 systolic HTN. A placebo run-in, patients (pts) (N=169) with seated SBP ≥160 and <200 mmHg and diastolic BP (DBP) <110 mmHg received OLM 20 mg/d for 3 wks. The regimen was modified at 3-wk intervals if BP remained ≥120/80 mmHg: up-titration of OLM to 40 mg/d; addition of HCTZ 12.5 mg/d; and up-titration of HCTZ to 25 mg/d. If pts’ BP remained ≥120/80 mmHg, they could enter a 4-wk extension phase, wherein HCTZ was increased to 50 mg/d. The primary endpoint was change from baseline in mean trough SBP after 12 wks of treatment. Mean age was 60 yrs, 46% of pts were male and 84% were non-black; mean baseline BP was 171/95 mmHg. Adverse event (AE) and metabolic data were tabulated for all pts who received ≥1 dose of study medication. Both OLM and HCTZ were well tolerated with a low incidence of AEs across the dosing range. Drug-related AEs occurring in ≥2% of pts included dizziness (OLM 40/HCTZ 12.5, 3.8%; OLM 40/HCTZ 25, 4.9%; OLM 40/HCTZ 50, 5.7%), increased γ-glutamyl transferase (OLM 40/HCTZ 25, 2.1%), increased serum uric acid (OLM 40/HCTZ 50, 7.6%), increased blood creatinine (OLM 40/HCTZ 25, 2.1%; OLM 40/HCTZ 50, 5.7%), increased blood urea (OLM 40/HCTZ 50, 7.6%) and fatigue (OLM 40/HCTZ 25, 2.1%). Symptomatic hypotension occurred in 1 pt (0.64%) with OLM 40/HCTZ 12.5 and 1 pt (0.94%) with OLM 40/HCTZ 50. Serum potassium, glucose and uric acid levels remained within normal limits for all OLM/HCTZ combinations (Table); no incidents of gout