

## Effectiveness of initiating treatment with valsartan/hydrochlorothiazide in patients with stage-1 or stage-2 hypertension

### BACKGROUND:

- Blood pressure control rates for patients with hypertension continue to be low and improvements in therapeutic management strategies are required in order for more patients to reach target blood pressure goals
- Combinations of antihypertensive agents are readily available, but their use remains low
- Earlier and more frequent use of combination therapy in the management of hypertension would greatly improve blood pressure control rates

### OBJECTIVE:

- To determine the efficacy of initial combination therapy with valsartan and HCTZ in patients with stage-1 or stage-2, uncomplicated hypertension as compared with initiating therapy with low or higher dose valsartan monotherapy

### METHODS:

- **Design:** 6 week, randomized, double-blind, parallel group controlled experimental trial
- **Inclusion/Exclusion criteria:**
  - Inclusion – patients age 18 or older with a documented diagnosis of hypertension (defined as a mean sitting systolic blood pressure  $\geq 150$  mmHg, but  $<180$  mmHg **AND** a mean sitting diastolic blood pressure  $\geq 90$  mmHg, but  $<110$  mmHg)
  - Exclusion – patients with severe hypertension; known or suspected secondary hypertension; previous myocardial infarction, stroke, or other cardiovascular complication; severe hepatic disease; history of malignancy; allergy or hypersensitivity to valsartan or hydrochlorothiazide; and pregnant women
- **Number of patients enrolled/drug regimens and dosages used**
  - Low dose valsartan (80mg daily) – 218
  - High dose valsartan (160mg daily) – 221
  - Valsartan/HCTZ combination (160mg/12.5mg daily) - 213
- **Primary outcome measure:**
  - Change in mean sitting systolic blood pressure from baseline
- **Secondary outcome measure:**
  - Time to achieve blood pressure goal (defined as first achievement of the target blood pressure goal of  $<140$  mmHg systolic blood pressure and  $<90$  mmHg diastolic blood pressure)
- **Power:**
  - To detect a change of 14 mmHg from baseline to week 4, a total sample size of 648 patients provided an 80% power to detect a statistically significant difference at the 0.05 level
- **Data handling method used:**
  - Intent to treat method of data handling was used

### RESULTS:

- **Number of patients who completed the study:**
  - 601 patients completed the study: v-low – 201, v-high – 204, v-combo - 196
- **Primary outcome measure:**
  - The proportion of patients achieving blood pressure control was higher for the v-combo group than the v-low or v-high group at weeks 2, 4, and 6 ( $p<0.05$ )

- **Secondary outcome measure:**
  - The time to goal was significantly improved in the v-combo ( $2.8 \pm 0.13$  weeks) as compared to the v-high ( $3.9 \pm 0.15$  weeks) and v-low ( $4.3 \pm 0.14$  weeks) in both stage-1 and stage-2 hypertension groups ( $p < 0.0001$ )
- **Authors stated conclusion:** Initiating therapy for hypertension with valsartan and low dose HCTZ (160/12.5mg) resulted in higher blood pressure control rates, greater antihypertensive effect, and prompt blood pressure control with no significant increase in adverse events in patients with stage-1 or stage-2 hypertension

#### STRENGTHS:

- Washout period for all pre-study antihypertensive medications prior to study drug administration
- Statistically significant differences found for all outcome measures
- Prohibition of concomitant therapy with medications known to alter blood pressure

#### LIMITATIONS:

- Investigators did not allow the drug to reach maximum antihypertensive effect before determining treatment failure and increasing dosage
- Short study duration
- Active control used
- Manufacturer involvement in study design, conduct, data collection, and data management
- No baseline information regarding previous antihypertensive regimens used by participants
- No distinction between stage-1 and stage-2 hypertension participant results

#### CONCLUSION:

- Treatment with valsartan/HCTZ combination therapy resulted in greater decreases in blood pressure, shorter time to blood pressure goal, and similar rates of adverse event occurrence and patient drop outs as compared to valsartan monotherapy
- Future research
  - Head to head trials with other antihypertensive regimens such as: beta blockers, calcium channel blockers, diuretics, angiotensin converting enzyme inhibitors, angiotensin II receptor blockers, and combination therapies
  - Trials need to be of sufficient length to allow for maximum antihypertensive effect of medications to be reached
  - Manufacturer involvement in the collection, management, and interpretation of study data must be limited
  - Trials in which patient population is limited to newly diagnosed, previously untreated, stage-1 hypertensive patients

**Reference:** Zappe DH, Palmer BP, Calhoun DA, Purkayastha D, Samuel R, and Jamerson KA. Effectiveness of initiating treatment with valsartan/hydrochlorothiazide in patients with stage-1 or stage-2 hypertension. *Journal of Human Hypertension*. 2010 Jul;24:483-491.