tion is obscure. Probably part of the decrease of heart rate can be explained by the lengthening of PQ-duration.

Key Words: Betablocking Agent, Electrocardiogram, Hypertension

P-222
GREATER EFFICACY OF CHLORTHALIDONE OVER HYDROCHLOROTHIAZIDE FOR ACHIEVING BLOOD PRESSURE GOALS
Nitin Khush, Dave Chua, William J Elliott, George L Bakeis. Medicine, Rush University Medical Center, Chicago, IL; Preventive Medicine, Rush University Medical Center, Chicago, IL.

Thiazide diuretics have gained renewed importance as antihypertensive agents following results of recent clinical trials and the JNC 7. While chlorthalidone (CTD) was utilized in all NIH-sponsored cardiovascular outcome trials, hydrochlorothiazide (HCTZ) remains the most commonly prescribed thiazide diuretic in the United States. The aim of this study was to determine the blood pressure (BP) lowering efficacy of CTD when substituted at the same milligram dose for HCTZ in patients who were not at goal BP i.e. <140/90 mmHg. A review of 2000 charts revealed 10 patients that were switched from HCTZ to CTD at identical doses. Differences in BP were calculated as change from BP on HCTZ to BP on CTD. Two supine BP readings were averaged and recorded from both the index visit, prior to the switch and first visit after the switch. BP’s were measured in the sitting position according the AHA guidelines.

Results: Patient characteristics included a mean age of 66±6 years, (6 females, 6 Caucasians and 4 African-Americans, 4 patients with dyslipidemia). Patients studied were receiving an average of 2.8 antihypertensive medications in addition to the thiazide diuretics. The average BP at the index visit on HCTZ was 157±14/80±11 mmHg. After an average of 64±12 days, the average BP on follow-up was 147±13/81±14 mmHg. Thus, CTD provided a greater reduction in BP by 10±6 mmHg (P<0.004) over HCTZ. Moreover, an additional 20% had achieved their target BP following the switch. These two patients had systolic BPs within 10 mmHg of goal BP while the others averaged 14±8 mmHg above the goal. Hypokalemia was not detected in any of those evaluated. The results of this observational study demonstrate that CTD has greater efficacy for lowering systolic BP compared to HCTZ. This further decrease in systolic BP by CTD argues for its use over HCTZ when goal BP is not achieved. The efficacy of CTD versus HCTZ needs further investigation.

Key Words: Hydrochlorothiazide, Systolic Pressure, Chlorthalidone

P-223
THE COMBINATION OF OLMESARTAN MEDOXOMIL PLUS HYDROCHLOROTHIAZIDE IN SUBJECTS WITH STAGE 2 HYPERTENSION: RESULTS OF A RANDOMIZED, DOUBLE-BLIND, FACTORIAL-DESIGN STUDY
John B Kostis, Tenuous Sifani. UMDNJ Robert Wood Johnson Medical School, New Brunswick, NJ; Medical and Scientific Affairs, Sankyo Pharma, Parsippany, NJ.

According to JNC 7 guidelines, patients classified as having stage 2 hypertension will likely require 2 or more agents to achieve blood pressure (BP) goals of <140/90 mm Hg (<130/80 mm Hg for patients with diabetes or chronic renal disease). A randomized, double-blind, factorial-design study in hypertensive patients demonstrated that the combination of olmesartan medoxomil/hydrochlorothiazide (OLM/HCTZ) provided substantial reductions in systolic blood pressure/diastolic blood pressure (SBP/DBP) that were significantly greater than monotherapy with either agent alone. To put these BP reductions into perspective, we assessed the BP control rates for this same population of patients. Five hundred two patients with a baseline mean seated DBP (SeDBP) of 100 to 115 mm Hg were randomized to placebo; OLM 10, 20, or 40 mg/day; HCTZ 12.5 or 25 mg/day; or OLM/HCTZ combination therapy. The primary efficacy variable was change from baseline in mean trough SeDBP at week 8. Secondary efficacy variables included the change from baseline in mean trough SeSBP; responder rates (SeDBP <90 mm Hg or ≥10 mm Hg reduction); and control rates (SeSBP <140 or <130; SeDBP <90 or <85 mm Hg). All combination doses resulted in substantial BP reductions. Treatment with OLM 40 mg, OLM 40 mg/HCTZ 12.5 mg, and OLM 40 mg/HCTZ 25 mg resulted in dose-dependent reductions of 16/15, 19/18, and 27/22 mm Hg, respectively (Table). The SeSBP control rate of <140 mm Hg was achieved by 60%, 62%, and 87% of subjects receiving OLM 40 mg, OLM 40 mg/HCTZ 12.5 mg, and OLM 40 mg/HCTZ 25 mg, respectively; and the SeDBP control rate of <90 mm Hg was achieved by 51%, 74%, and 80% of subjects given OLM 40 mg, OLM 40 mg/HCTZ 12.5 mg, and OLM 40 mg/HCTZ 25 mg, respectively. An assessment of the more rigorous control rate of <130 mm Hg or <85 mm Hg demonstrated that nearly two thirds of subjects reached goal on OLM 40 mg/HCTZ 25 mg. The overall incidence of adverse events was similar to placebo. These results demonstrate that the combination of OLM/HCTZ is a safe and highly effective treatment option for stage 2 hypertension.

Key Words: Olmesartan, Hydrochlorothiazide, JNC 7 and Stage 2 Hypertension

P-224
PERSISTENCE AND ADHERENCE TO ANTIHYPERTENSIVE AGENTS
Jean Lachaine, Farzad Ali, Elizabeth Merikle. Faculty of Pharmacy, University of Montreal, Montreal, QC, Canada; Pfizer Canada Inc., Kirkland, QC, Canada.

Background: There is a lot of debate about the selection of the most appropriate treatments for hypertension. Most treatment recommendations are based on criteria that consider efficacy, safety and cost. Given the need for long-term utilization of these agents, treatment compliance should also be taken into consideration in the selection process.

Objective: The purpose of this study was to estimate persistence and adherence to antihypertensive agents in a real life setting.

Methods: This study was performed using data from the Regie de l’assurance maladie du Quebec (RAMQ). Persistence and adherence to treatment were estimated separately and an index combining these two measures was calculated. Persistence to treatment was calculated as the proportion of patients who had not definitively abandoned their treatment two years after they started it. Adherence to treatment was calculated as the proportion of patients for whom the ratio of the quantity of medication received over the quantity needed for the treatment period was above 80%. The persistence-adherence index was calculated by multiplying the monthly persistence rates by the monthly adherence rates over a two-year period.

Results: Data from a random sample of 64,175 subjects covered by the RAMQ drug plan and one of the antihypertensive agent reimbursed by the drug plan for the first time between January 1999 and December 2000 were analysed. After a two-year period, persistence to treatment varied across antihypertensive agents. Persistence rates to β-blockers, amlodipine, angiotensin II receptor antagonists, other calcium channel blockers, ACE inhibitors, other diuretics, hydrochlorothiazide, and chlorthalidone
were 71%, 67%, 66%, 64%, 63%, 60%, 52% and 23% respectively. The persistence-adherence index at two year was 66% for ARAs, 63% for amlopidine, 62% for β-blockers, 61% for other CCBs, 60% for ACE inhibitors, 51% for hydrochlorothiazide, 50% for other diuretics and 32% for chlorothalidone.

**Conclusion:** Persistence and adherence to treatment are essential to treatment success and varied substantially between the different therapeutic options. Results of this study indicate that, in a real life setting, patients are significantly less compliant to diuretics than to any other antihypertensive agents.

**Key Words:** Treatment Compliance, Antihypertensive Drugs, Drug Databases Analyses

P-225

**EFFECTIVE BLOOD-PRESSURE CONTROL WITH VALSARTAN/HCTZ COMBINATION THERAPY IN PATIENTS WITH MODERATE TO SEVERE SYSTOLIC HYPERTENSION: THE VALOR TRIAL**

_Yves Lacourciere, Daniëlle Hebert, Linda Assouline, Bonita Rehel, Yasser Khider. Director Hypertension Unit, Centre Hospitalier Universite Laval, Sainte Foy, QC, Canada; Medical Department, Novartis Pharma Canada inc., Dorval, QC, Canada; Clinical Development & Medical Affairs, WSJ-202.228A Novartis, Basel, Switzerland.

**Background:** Increasing evidence shows that combination therapy with at least two antihypertensive agents is needed to achieve appropriate blood-pressure (BP) control in a large part of the hypertensive population. One of the most appealing combinations is that of adding a diuretic to an angiotensin-receptor blocker (ARB).

**Methods:** We studied the effects on siting systolic BP of the combinations valsartan (V; an ARB) 160 mg + HCTZ 12.5 mg and V160 mg + HCTZ 25 mg od, compared with monotherapy V160 mg od. Treatment-naïve and previously treated patients (N=767) with moderate to severe systolic hypertension (SBP ≥160 mm Hg and ≥200 mmHg) and with or without co-morbidities, were randomised (after a 2-week washout if previously treated and a 2 week placebo run-in period) to either V80 od (monotherapy group) or V160 od (combination groups) for 4 weeks, with force-tration to V160 mg, V160/HCTZ 12.5 od or V160/HCTZ 25 od for an additional 4 weeks. Endpoints were change in SBP between V160 and V160/HCTZ 25 and between V160/HCTZ 12.5 and V160; changes in DBP between groups, response rates and tolerability.

**Results:** As shown in the Table, all treatments were highly effective and there were additional SBP and DBP reductions in the combination groups. Responder rates were above 50% in all groups and reached 75% and there were additional SBP and DBP reductions in the combination V160/HCTZ 25 od and with or without co-morbidities, were randomised (after a 2-week washout if previously treated and a 2 week placebo run-in period) to either V80 od (monotherapy group) or V160 od (combination groups) for 4 weeks, with force-tration to V160 mg, V160/HCTZ 12.5 od or V160/HCTZ 25 od for an additional 4 weeks. Endpoints were change in SBP between V160 and V160/HCTZ 25 and between V160/HCTZ 12.5 and V160; changes in DBP between groups, response rates and tolerability.

**Conclusions:** V160 mg od is safe and effective in patients with moderate to severe systolic hypertension. Adding HCTZ 12.5 or 25 mg provides significant additional reductions in systolic and diastolic BP and increases responder rates compared with V160 mg monotherapy, with maintained excellent tolerability.

**Table 1**

<table>
<thead>
<tr>
<th></th>
<th>V160</th>
<th>V160/HCTZ12.5</th>
<th>V160/HCTZ25</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>261</td>
<td>254</td>
<td>252</td>
</tr>
<tr>
<td>Male/female</td>
<td>130/131</td>
<td>141/113</td>
<td>140/112</td>
</tr>
<tr>
<td>Mean age</td>
<td>60.4 (10.6)</td>
<td>60.8 (11.5)</td>
<td>60.7 (11.6)</td>
</tr>
<tr>
<td>Mean SBP</td>
<td>167.9 (8.0)</td>
<td>167.4 (8.3)</td>
<td>167.2 (7.9)</td>
</tr>
<tr>
<td>Baseline mean SBP/DBP</td>
<td>167.9 (8.0)/93.2 (8.9)</td>
<td>167.4 (8.3)/93.4 (9.6)</td>
<td>167.2 (7.9)/93.7 (8.8)</td>
</tr>
<tr>
<td>Mean change SBP/DBP</td>
<td>−20.7 (15.7)/−4.6 (8.9)</td>
<td>−27.9 (13.9)/−10.2 (7.7)*</td>
<td>−28.6 (13.5)/−10.1 (7.6)*</td>
</tr>
<tr>
<td>Response rate%</td>
<td>56.9%</td>
<td>74.4%*</td>
<td>75%*</td>
</tr>
<tr>
<td>Any AE (monotherapy phase)</td>
<td>37.3%/27.5%</td>
<td>32.1%/28.6%</td>
<td>32.8%/34.0%</td>
</tr>
<tr>
<td>Any AE (combination phase)</td>
<td>46.9%/37.5%</td>
<td>41.4%/36.7%</td>
<td>42.2%/37.9%</td>
</tr>
</tbody>
</table>

Values in brackets are ± SD. * P < 0.05 vs V160; † SBP < 140 or decrease in SBP ≥20 mmHg and/or DBP<50 mmHg

Key Words: Valsartan, Combination Therapy, Double-Digit Blood-Pressure Lowering Efficacy