Aliskiren-Based Therapy Controls Blood Pressure Regardless of Plasma Renin Activity

Aliskiren, a direct renin inhibitor, provides effective blood pressure (BP) control in combination with hydrochlorothiazide (HCTZ) and amlodipine regardless of baseline plasma renin activity (PRA) in patients with hypertension, according to findings from a new study. Aliskiren was well tolerated as monotherapy and when used in combination with other antihypertensive medications.

Although aliskiren is established as an effective antihypertensive agent, it is not known whether its BP-lowering effects are dependent on baseline PRA levels. The current study was defined to evaluate the ability of aliskiren to control BP alone and in combination with other antihypertensive medications in patients with various baseline PRA levels. Dominique Richter, MD, Jarny, France, presented findings of the prospective, open-label trial.

The study included 256 patients with elevated systolic (140 mm Hg to 179 mm Hg) and diastolic (90 mm Hg to 109 mm Hg) BP. After an optional washout period and a placebo run-in period, all patients started active treatment with aliskiren at a dose of 150 mg once daily. Patients who did not achieve BP targets after 4 weeks received increasingly aggressive therapy, including the addition of HCTZ and amlodipine, at 4-week intervals for a maximum of 6 treatment periods until the goal BP was attained.

The primary endpoint was the percentage of patients achieving BP targets, defined as <140/90 mm Hg for non-diabetic subjects or <130/80 mm Hg in those subjects with diabetes. Systolic BP (SBP) and diastolic BP (DBP) responses were also defined as reductions of ≥20 mm Hg and ≥10 mm Hg from baseline, respectively.

Patients had a variety of cardiovascular risk factors at baseline, including obesity (37.1%), diabetes (34.4%), moderate hypertension (44.5%), and renal impairment (7.4%). The mean patient age was 55.4 years, and the mean seated BP was 156/92 mm Hg. In this analysis, patients were stratified according to baseline PRA level, defined as low (≤0.65 ng/ml/hr) or moderate to high (>0.65 ng/ml/hr).

Overall, 87% of patients achieved target BP levels with the most intensive regimen, which consisted of aliskiren, HCTZ, and amlodipine. BP control with triple combination therapy was equally effective across patient groups, including those with low PRA (87%) and moderate to high PRA (87%) at baseline. In addition, combination therapy with aliskiren, HCTZ, and amlodipine resulted in a SBP response in 96% to 97% of patients and a strong DBP responses in 96% to 100% of patients. By comparison, 30% to 60% of patients achieved BP responses with aliskiren monotherapy, and 68% to 89% of patients achieved BP responses with aliskiren plus HCTZ.

Aliskiren was well tolerated as monotherapy and in combination with other antihypertensive medications. The overall adverse event rate was 14.8% in the aliskiren monotherapy group, 12.2% in the aliskiren plus HCTZ group, and 6.7% in the triple combination therapy group. First-line treatment with aliskiren, with the addition of HCTZ and amlodipine as needed, provides an important treatment option for clinicians involved in the management of patients with hypertension, Dr. Richter concluded.

A Different Analytic Approach to Assess J-Curve Findings from the FEVER Trial

When taking a detailed look at the J-shaped relation between an increased risk of cardiovascular (CV) events and achieved systolic and diastolic blood pressure (BP) <120/70 mm Hg, investigators concluded that the J-curve is a real phenomenon based on further analysis of the FEVER data. Xuezhong Zhang, MD, Clinical Trials and Research Center, Chinese Hypertension League, Beijing, China, presented findings from this innovative approach to the FEVER data.

There is some debate as to optimal BP goals on drug therapy due to the absence of consistent trial data. In fact, such goals are often determined as a consequence of correlating events found in post-hoc analyses. There is some variation among these post-hoc analyses, but there has been some suggestion that a J-curve may exist in which the risk of CV events increases when achieved BP is below 120/70 mm Hg. However, this suggestion is based on a limited number of subjects and outcomes within the larger study which may cloud the analytical accuracy of the findings.

In FEVER, patients were stratified according to their mean on-treatment BP, regardless of therapeutic regimen, and CV events in each group were estimated. The ranges of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were as follows: ≤110, >110-120, >120-130, >130-140, >140-150, >150-160, and >160 mm Hg for SBP; ≤60, >60-70, >70-80, >80-90, >90-100, and >100 mm Hg for DBP.

A total of 9711 patients were randomized. Over 60 follow-up months, 159,844 BP measurements were performed with 3 SBP and 3 DBP readings over 30 minutes at each observation. Mean SBP and DBP values were calculated based on overall follow-up time.

During further analysis of the study data, investigators took a different analytical approach in order to reveal the nature of the J-curve phenomenon. This approach evaluated moving events per 1000 patient observations (MEPPO) instead of applying the previous overall means methodology. Analysis was then based on observations from each visit in which event and BP data was collected. Therefore, event data corresponded with BP measured prior to the visits. Zhang and colleagues also limited the previously broad 10 mm Hg range to which events were referred to 1 mm Hg steps. This allows for each observation to enter 10 times into 10 consecutive 10 mm Hg BP ranges. Thus, the overall number of analyzed data is greatly increased.

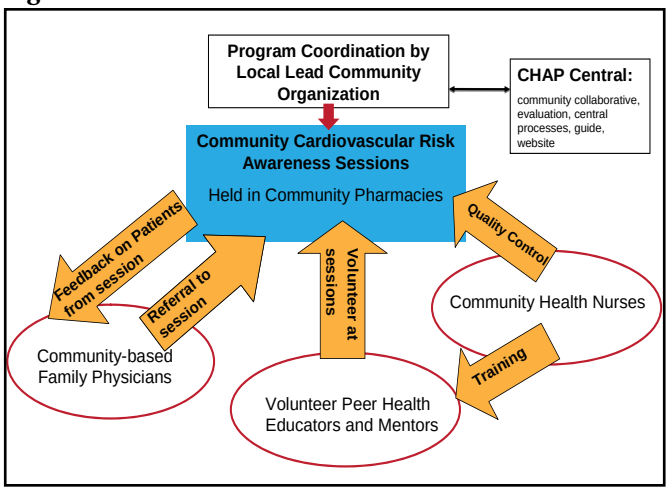
Using this methodology, the J-curve phenomenon was determined to be genuine. After adjusting for baseline risks, the risk of CV events correlated with SBP of 129 mm Hg to 139 mm Hg and DBP of 79 mm Hg to 86 mm Hg in the FEVER trial. The lowest point of the J-curve was consistent with and without adjustments. These are important findings with regards to optimal BP goals in patients receiving drug therapy for hypertension.

An Innovative Approach to Cardiovascular Risk Reduction: Results from the C-CHAP Study

A community outreach program aimed at improving cardiovascular (CV) health awareness is an effective, feasible approach to CV management and risk reduction, according to results from the Community Cardiovascular Health Awareness Program (C-CHAP). Lisa Dolovich, BScPhm, MSc, PharmD, McMaster University, Hamilton, Ontario, Canada, presented results from this Canadian community cluster, randomized, controlled trial.

C-CHAP was designed to evaluate the effectiveness of a CV health awareness program in reducing the incidence of stroke and CV morbidity at the community level (population 10,000 to 60,000). Randomization included 39 communities with participating family physicians and pharmacists, of which 20 received intervention. C-CHAP intervention consisted of community-wide CHAP session promotion, trained peer volunteers who monitored blood pressure (BP) measurements (via an automated device) and administered standardized CVD and stroke risk assessments, and local educational resources targeting specific modifiable risk factors were provided to all participants (Figure 1). BP and risk assessment data were entered into a centralized, web-based data management system and was disclosed to clinicians and participants. Community health nurses and pharmacists were made available to those participants who had high BP readings and follow-up was arranged for those participants who were deemed high-risk. CHAP education sessions were held on a weekly basis for all participants.

Figure 1. How CHAP Works.



In the fall of 2006, CHAP was successfully launched in 20 randomly selected communities with 214 active physician participants and 129 active pharmacy participants. Assessments were performed on 15,889 unique participants and 1265 sessions took place (~25% of older adults attended at least one session). Pre- and post-CHAP data were documented and analyzed (defined as 01/09/2005-31/08/2006 and 01/09/2007-31/08/2008, respectively).

The primary composite end-point was the rate of hospital admissions for acute myocardial infarction (AMI), congestive heart failure (CHF), and stroke among community residents aged ≥65 years. A significant decrease in hospital admissions for the composite endpoint was observed in the CHAP group compared with control (RR, 0.91; 95% CI, 0.86 to 0.97; p<0.01). The CHAP communities demonstrated a 6% decrease in hospital admissions during the aforementioned time period, while the control communities demonstrated a 3% increase. The rate of hospital admissions for AMI and CHF also favored the CHAP approach compared with control (p<0.01 for AMI and p=0.03 for CHF). CHAP resulted in lower rates of in-hospital death (p=0.06) and fewer instances of hypertension therapy initiation (p=0.02).

This innovative approach to CV risk reduction resulted in significant decreases in CV morbidity. It appeared to be