CAPABLE: Clinical Utility of Caduet in Simultaneously Achieving Blood Pressure and Lipid Endpoints in a Specific Patient Population

Disclosures

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New data presented at the 2006 American Society of Hypertension annual meeting in New York support the efficacy of a fixed-dose therapy combining a calcium antagonist (amlodipine) and a statin (atorvastatin) for addressing the principal cardiovascular risk factors in African Americans. According to the trial's lead investigator, John Flack, MD, the Clinical utility of Caduet in simultaneously Achieving Blood Pressure and Lipid Endpoints in a specific patient population (CAPABLE) study[1] has provided "further evidence for the broad clinical utility of the single pill amlodipine/atorvastatin combination by showing that it can effectively target the most important, modifiable risk factors in African American patients." In addition, the combination pill has a safety profile "that is very reasonable."

Rationale

African Americans have the highest overall mortality rate from coronary heart disease (CHD) of any ethnic group in the United States and almost double the risk of experiencing a stroke compared with whites. Recent data have demonstrated that the levels of treatment and control of hypertension and dyslipidemia are worse among African Americans than in whites. Management of the risk for cardiovascular disease events through lowering blood pressure and cholesterol levels in African Americans is therefore a major challenge that needs to be addressed.

A single pill combining amlodipine and atorvastatin at various fixed doses has been available in the United States since 2004 as Caduet (Pfizer, New York, NY). Clinical studies with this combination have shown that it is an effective and well-tolerated method of helping patients simultaneously lower both blood pressure and low-density lipoprotein (LDL)-cholesterol. A post-hoc analysis of the Gemini study,[2] a 14-week, open-label, noncomparative trial of amlodipine/atorvastatin, demonstrated that the single-pill therapy was effective in reducing blood pressure and LDL-cholesterol among a population of African American patients who were not previously at goal for either hypertension or dyslipidemia. About 44% of patients in Gemini attained both blood pressure and LDL-cholesterol goals.
To follow up on these results, CAPABLE was set up as a 20-week, open-label, comparative, multicenter trial to further evaluate the efficacy, safety, and utility of using amlodipine/atorvastatin in a high-risk population of African Americans with concomitant dyslipidemia and hypertension.

**Patients**

All patients were self-identified African Americans aged 18-80 years with hypertension and dyslipidemia (treated or untreated), not at goal for blood pressure, and either at LDL-cholesterol goal with medication or not at goal with or without medication. Patients were excluded if they were already taking either amlodipine or atorvastatin or the fixed combination.

A total of 494 patients were allocated to 3 cardiovascular risk groups. Patients in Group I (n = 89) had hypertension plus dyslipidemia and no other cardiovascular risk factors. Groups II (n = 161) and III (n = 244) had hypertension and dyslipidemia plus ≥ 1 of the following other cardiovascular risk factors:

- Age ≥ 45 years (men) or ≥ 55 years (women)
- Premature CHD in first-degree relative
- Current smoker
- High-density lipoprotein (HDL)-cholesterol < 40 mg/dL (or > 60 mg/dL)

Patients in Group III also had CHD or risk equivalent (diabetes mellitus or any atherosclerotic disease).

At baseline, blood pressure was similar in all 3 groups, although systolic blood pressure (SBP) and diastolic blood pressure (DBP) were both lower in Group III (Table 1). About 50% of patients overall had uncontrolled LDL-cholesterol levels at baseline (approximately 9% in Group I, 50% in Group II, and 60% in Group III).

**Table 1. Baseline Values**

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure (mm Hg)</td>
<td>147.9/93.7</td>
<td>149.1/93.7</td>
<td>&lt; 146.0/88.6</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dL):</td>
<td>160.0</td>
<td>151.4</td>
<td>129.3</td>
</tr>
<tr>
<td>ITT population</td>
<td>185.5</td>
<td>170.4</td>
<td>142.0</td>
</tr>
</tbody>
</table>
ITT = intention to treat; LDL = low-density lipoprotein

Treatment

There was no washout of baseline antihypertensive or lipid-lowering medications. Treatment with amlodipine/atorvastatin over 20 weeks consisted of flexible titration using 8 fixed-dosage strengths: 5/10 mg, 5/20 mg, 5/40 mg, 5/80 mg, 10/10 mg, 10/20 mg, 10/40 mg, and 10/80 mg. Amlodipine/atorvastatin was integrated into existing antihypertensive and lipid-lowering treatment strategies or initiated as sole treatment. Counseling was provided about lifestyle modification, although this was not an aggressive program, Dr. Flack stressed.

Blood pressure goals were based on recommendations in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), and LDL-cholesterol goals were based on recommendations in the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) (Table 2).

Table 2. Treatment Goals

<table>
<thead>
<tr>
<th>Goal</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure (mm Hg)</td>
<td>&lt; 140/90</td>
<td>&lt; 140/90</td>
<td>&lt; 130/80</td>
</tr>
<tr>
<td>LDL-cholesterol goal (mg/dL)</td>
<td>&lt; 160</td>
<td>&lt; 130</td>
<td>&lt; 100</td>
</tr>
</tbody>
</table>

LDL = low-density lipoprotein

The blood pressure goal was focused mainly on SBP, since SBP is a more important determinant of cardiovascular risk and more easily measured accurately than DBP, Dr. Flack explained.

Outcomes

Overall, about 48% of patients achieved both blood pressure and LDL-cholesterol goals at Week 20; this was the primary outcome of the study (Table 3). Groups I and II had the highest rates of patients achieving individual blood pressure and LDL-cholesterol goals, as well as both goals combined, compared with Group III, despite lower baseline levels in Group III.

Table 3. Goal Attainment (%) (ITT population)

<table>
<thead>
<tr>
<th>Goal</th>
<th>All Groups</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCEP ATP III</td>
<td>73.7</td>
<td>89.9</td>
<td>87.4</td>
<td>58.7</td>
</tr>
</tbody>
</table>
Similar trends in blood pressure goal achievement were seen in the patients who had uncontrolled LDL-cholesterol at baseline, but more of the patients (over 50%) in Group III achieved an LDL-cholesterol goal of < 100 mg/dL (Table 4).

Table 4. Goal Attainment (%) in Patients With Baseline Uncontrolled LDL-Cholesterol

<table>
<thead>
<tr>
<th>Goal</th>
<th>All Groups</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCEP ATP III</td>
<td>68.5</td>
<td>88.0</td>
<td>84.4</td>
<td>53.8</td>
</tr>
<tr>
<td>JNC 7</td>
<td>54.5</td>
<td>70.0</td>
<td>70.9</td>
<td>40.5</td>
</tr>
<tr>
<td>NCEP ATP III + JNC 7</td>
<td>43.6</td>
<td>62.4</td>
<td>62.4</td>
<td>26.2</td>
</tr>
<tr>
<td>LDL-cholesterol &lt; 100 mg/dL</td>
<td>44.6</td>
<td>20.0</td>
<td>40.4</td>
<td>53.8</td>
</tr>
</tbody>
</table>

The overall mean percentage reduction in LDL-cholesterol was 23.6% (23%, 30%, and 20.1% in Groups I, II, and III, respectively) (range, 27%-34% in Groups I-III). The reduction in LDL-cholesterol was greater in the patients whose LDL-cholesterol was uncontrolled at baseline, at 31% overall. Mean overall reduction in total cholesterol was 17%, with changes of 6.9% in triglycerides, 6.0% in very low-density lipoprotein, 19.3% in apolipoprotein B (ApoB), and an overall 2.2% increase in HDL-cholesterol. Similar trends were seen in the patients with uncontrolled LDL-cholesterol at baseline. Blood pressure changes were similar in all groups (-17 to -18 mm Hg SBP and -10 to -11 mm Hg DBP).

Safety

Thirty-four patients (6.8%) discontinued treatment due to adverse events. The most common events that led to discontinuation were headache (1%), myalgia (0.6%), elevated liver function tests (0.6%), and arthralgia (0.6%). All of these events were mild to moderate in severity. There were no
unexpected or serious adverse events.

Implications

About half of the patients in CAPABLE overall achieved both blood pressure and LDL-cholesterol goals, including two thirds of patients in Groups I and II, but less than one third of patients in Group III. About 75% of patients reached their LDL-cholesterol goal and more than 50% reached their blood pressure goal. Along with its "excellent safety profile in this population," the CAPABLE data show that amlodipine/atorvastatin alone or with additional antihypertensive therapy is effective and well tolerated in African Americans with concomitant dyslipidemia and hypertension, Dr. Flack believes.

*The CAPABLE study was supported by Pfizer.*

References


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