OR-20
DETERMINANTS OF BLOOD PRESSURE RESPONSE TO ACE INHIBITOR MONOTHERAPY IN HYPERTENSIVE AFRICAN AMERICANS AND CAUCASIANS
Evan Mokwe, Suzanne E Ominit, Amanda I Dudley, John M Flack. Internal Medicine, Wayne State University, Detroit, MI.

Objectives: Data collected during a clinical trial evaluating rapidity of medication up-titration with blood pressure (BP) response were used to investigate multiple factors, including race, as predictors of blood pressure (BP) response to monotherapy with the ACE inhibitor, quinapril.

Methods: Participants with JNC-VI stages 1 or 2 hypertension (SBP 140–169 or DBP 90–104) were randomly assigned to fast (every 2 weeks; duration 6 weeks) or slow (every 6 weeks; duration 18 weeks) drug titration. Participants received 20 mg of quinapril once daily at randomization; at intervention-specific (fast or slow) follow-up visits, medication dose was doubled (up to 80 mg/day) if BP remained ≥ 140/90 mm Hg. Means and interquartile ranges (IQR, middle 50% of the SBP response distribution) were determined and compared by race. Factors associated with SBP responses in the lower 25% or the upper 25% of the response distributions were determined in multivariate logistic regression models.

Results: Data were available for 533 African Americans and 2,046 Caucasians; 53% of participants were women. Participant mean age was 51 years, and 48% were obese (BMI ≥ 30). Mean SBP responses were -10.5 ± 13.4 and -15.3 ± 12.2 mm Hg, respectively, in African Americans and Caucasians. IQR boundaries were -2.2 to -20 and -7.3 to -23.5 mm Hg in African Americans and Caucasians, respectively; these IQR were 3.7 and 3.4 times, respectively, larger than the racial difference in SBP response (4.8 mm Hg). Factors associated with BP response in the lower 25% of the SBP response distribution included fast treatment group (p = .06), early study visits (time), older age, African American race, obesity, higher medication dose, and lower baseline SBP (all p < .01). Factors associated with BP response in the upper 25% of the SBP response distribution included slow treatment group, later study visits (time), younger age, Caucasian race, lower medication dose and higher baseline SBP (all p < .01).

Conclusions: Racial difference in SBP response to treatment was documented even though the middle 50% of the SBP response distribution in both groups largely overlapped. Within-race IQRs of SBP response were several-fold greater than the mean difference in SBP response between the races. Race, along with other factors that vary at the level of the individual, predict extreme SBP responses to monotherapy with the ACE inhibitor quinapril.

Key Words: Blood Pressure Response, Ace Inhibitor, African American Race

OR-21
RELATION OF SERUM URIC ACID TO CARDIOVASCULAR ENDPOINTS IN HYPERTENSION: THE LIFE STUDY
Aud Høiegen, Sverre E Kjeldsen, Stevo Julius, Richard B DeVereaux, Michael Alderman, Cong Chen, Bjorn Dahlof. Div. Nephrology, Ullevaal University Hospital, Oslo, Norway; Department of Cardiology, Ullevaal University Hospital, Oslo, Norway; Department of Internal Medicine, Division of Hypertension, University of Michigan, Ann Arbor, MI; Division of Cardiology, Cornell Medical Center, New York City, NY; Department of Epidemiology and Social Medicine, Albert Einstein College of Medicine, New York City, NY; Merck Research Laboratories, Merck & Co., Blue Bell, PA; Department of Medicine, Sahlgrenska Hospital/Ostra, Gothenburg, Sweden.

Serum uric acid (SUA) has been proposed to be an independent risk factor for cardiovascular morbidity and death. Losartan is uricosuric, in contrast to atenolol and to other ARBs. The LIFE study was a double-masked, randomized, parallel-group trial in 9,193 patients (54% female) with essential hypertension and left ventricular hypertrophy. The participants received once-daily losartan- or atenolol-based treatment. We used Cox regression analysis to compare regimens.

Baseline SUA was significantly associated with increased cardiovascular risk (hazard ratio [HR] = 1.024 [95% CI, 1.017–1.032] per 10 μmol/L, p < 0.0001) with evidence of a significant gender interaction. Baseline SUA remained significantly associated with increased risk in women (HR = 1.025 [1.013–1.037], p < 0.0001) but not in men (HR = 1.009 [0.998-1.019], p = 0.108). After adjustment for Framingham risk score (FRS), SUA was no longer significant in the entire study population (HR = 1.006 [0.995-1.014], p = 0.122) or in men (HR = 1.006 [0.995-1.017], p = 0.291) but independently predicted composite endpoints in women (HR = 1.013 [1.005], p = 0.0957). The baseline-to-end-of-study increase in SUA (standard deviation, SD) differed between the treatment groups, 44.4 (72.5) μmol/L atenolol and 17.0 (69.8) μmol/L losartan, p < 0.0001. The contribution of SUA to the treatment effect of losartan in terms of the primary composite endpoint was 29% [14, 107], p = 0.004. Although the SUA-by-gender interaction was not significant (p = 0.079), the association between time-varying SUA and increased cardiovascular risk tended to be stronger in women (p < 0.0001) than in men (p = 0.0695).

In conclusion, treatment with losartan significantly attenuated the increase in SUA compared with treatment with atenolol in the LIFE study. This difference seemed to explain 29% of the treatment effect on the primary composite endpoint. Correlation between SUA and FRS, especially in men, complicates the interpretation. Further investigations are warranted.

Key Words: serum uric acid, losartan, risk factors

OR-22
CARDIOVASCULAR EVENTS DURING INITIAL ANTIHYPERTENSIVE THERAPY WITH EITHER A CALCIUM ANTAGONIST OR A DIURETIC/BETA-BLOCKER: META-ANALYSIS OF 7 CLINICAL TRIALS
William I. Elliott, Preventive Medicine, RUSH Medical College, Chicago, IL.

Despite the proven benefits of a low-dose diuretic or beta-blocker as initial antihypertensive therapy, recent prescription monitoring data show that a calcium antagonist remains very popular in this role. Several large clinical trials directly comparing representatives of these drug classes have released their results only recently, and these have not as yet been aggregated. We therefore gathered data from 7 trials (MIDAS, INSIGHT, NORDIL, NICS-EH, STOP-Hypertension 2, VHAS, CONVINCE) that directly compared a calcium antagonist against either a diuretic or beta-blocker as initial therapy across several cardiovascular (CV) endpoints, including myocardial infarction (MI) and congestive heart failure (CHF). Data from each trial report were combined using the Mantel-Haentzel method to give a relative risk and a 95% confidence interval (CI). Final data from ALLHAT were embargoed at the time of this submission, but will be included in May. The number of patients with events/number of patients in each group, and the results of the meta-analysis were:

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Calcium Antagonist</th>
<th>Diuretic/Beta-Blocker</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td></td>
<td>1.03 (0.94–1.12)</td>
<td></td>
</tr>
<tr>
<td>CV Death</td>
<td></td>
<td>1.06 (0.94–1.20)</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td>0.92 (0.81–1.03)</td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td></td>
<td>1.07 (0.95–1.21)</td>
<td></td>
</tr>
<tr>
<td>Major CV Events</td>
<td>1.01 (0.93–1.09)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHF</td>
<td>1.19 (1.02–1.38)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

These data indicate that, for all cardiovascular events except CHF, the relative risk for an initial calcium antagonist was not significantly dif-