Hypothesis: In hypertensive patients at high cardiovascular risk, for the same level of blood pressure control, valsartan will be more effective than amlodipine in reducing cardiac morbidity and mortality.

Methods: multi-country, randomized, DB, parallel-group comparison of valsartan vs amlodipine based Tx in high risk patients (n=15,245) >50yo followed up for ~4.2 yrs.

Results: BP reduced by both treatments but amlodipine based regimen lowered BP more-earlier in the study. Primary Composite endpoint HR 1.04 (p=0.49).


VALUE: Systolic Blood Pressure in Study

Sitting SBP by Time and Treatment Group

Difference in SBP Between Valsartan and Amlodipine

12 4 4 82 3 4 6 12 18 30 36 42 54 60 66

VALUE: Primary Composite Cardiac Endpoint

Proportion of Patients With First Event (%)

Number at risk

Valsartan
Amlodipine

VALUE: Fatal and Non-Fatal Myocardial Infarction 2° endpoint

Proportion of Patients With First Event (%)

Number at risk

Valsartan
Amlodipine

VALUE: Incidence of New-onset Diabetes 2° endpoint

23% Risk Reduction With Valsartan

P < 0.0001

VALUES: Outcome and SBP Differences at Specific Time Periods: Myocardial Infarction

Myocardial Infarction Odds Ratios and 95% CIs

Overall study 2.2
0-3 3.8
3-6 2.3
6-12 2.0
12-24 1.8
24-36 1.6
36-48 1.4
Study end 1.7

0.25 0.5 1.0 2.0 4.0
**VALUE: Tolerability**

<table>
<thead>
<tr>
<th></th>
<th>Valsartan (%)</th>
<th>Amlodipine (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinuations due to AE</td>
<td>13.4</td>
<td>14.5</td>
<td>0.045</td>
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<tr>
<td>Prespecified adverse events</td>
<td></td>
<td></td>
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<tr>
<td>Peripheral Oedema</td>
<td>14.9</td>
<td>32.9</td>
<td>&lt;0.0001</td>
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<tr>
<td>Dizziness</td>
<td>16.5</td>
<td>14.3</td>
<td>&lt;0.0001</td>
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<tr>
<td>Headache</td>
<td>15.2</td>
<td>12.9</td>
<td>&lt;0.0001</td>
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<tr>
<td>Additional common adverse events</td>
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<td></td>
<td></td>
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<tr>
<td>Diarrhoea*</td>
<td>8.8</td>
<td>6.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Angina Pectoris*</td>
<td>9.3</td>
<td>6.4</td>
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<tr>
<td>Angina Pectoris†</td>
<td>4.4</td>
<td>3.1</td>
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<tr>
<td>Oedema Other*</td>
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<tr>
<td>Hypokalaemia*</td>
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<td>6.2</td>
<td>&lt;0.0001</td>
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<tr>
<td>Atrial Fibrillation†</td>
<td>2.4</td>
<td>2.0</td>
<td>0.1197</td>
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<tr>
<td>Syncope†</td>
<td>1.7</td>
<td>1.0</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*With an incidence >3% and a difference between treatment groups >1%.
†Reported as serious.

**VALUE**

Summary: Good BP control was achieved with both treatment regimens, but BP decrease in the amlodipine group was more pronounced, particularly early in the trial. Despite blood pressure differences, the primary composite cardiac endpoint was not different between the treatment groups.

Interpretation: No difference in main outcomes, however unequal reductions in BP may account for differences between groups in cause-specific outcomes. Prompt BP control is important in high risk hypertensives.