Angiotensin-receptor blockade versus converting-enzyme inhibition in type 2 diabetes and nephropathy (DETAIL Study)

Study Type: DOE
Purpose: Compare the effect of telmisartan and enalapril on the change in GFR.
Study Duration: 5 years
Trial Design: multicenter (39 centers in northern Europe), randomized, double-blind, double-dummy,
one-month's screening included an ACE-inhibitor, then randomization, after 2 months other meds could be used to reduce pressure if needed
Medications: telmisartan 40 mg vs enalapril 10 mg with forced titration to telmisartan 80 mg vs enalapril 20 mg all given as a daily
Patients: 72% male, mean age 60 yrs, 98% white, BMI ~ 31, baseline sitting BP ~152/86, pulse = 74, 21% smoke, 75% drink modest
History: mean yrs of duration - HTN 8 yrs, diabetes 8 yrs, 50% have a history of cardiac disease, 52% beta-blockers, 46% CCB, 18% ASA, 42% statin
Baseline labs: CrCl = ~92, SCr = 1, urinary albumin excretion rate was 46 in telmisartan grp and 60 in enalapril grp, 82% with microalbuminuria, 18% with proteinuria, TC = 224, LDL = 136, HDL = 48, TG = 210, HbA1c = 8.4
Inclusion: age 35-80, type 2 diabetes with treatment for at least a year with any combination (including insulin), mild to moderate HTN of less than 180/95, normal renal morphology, microalbuminuria between 11 and 999 mcg/min , SCr = < 1.6, HbA1c < 12, CrCl > 70
Exclusion: any condition other than cardiovascular disease that could limit survival
Primary endpoint: change in GFR at 5 years
Secondary endpoints: annual change in GFR, urinary albumin excretion, SCr level, BP, rate of clinical events, all-cause death rate

1. Are the results valid?
   * randomized? yes
   * double-blinded? yes
   * placebo-controlled? no, but comparative trial
   * patient accountability? yes
   * were groups similar? yes

2. What were the results?

<table>
<thead>
<tr>
<th>Primary endpoints</th>
<th>Telmisartan</th>
<th>Enalapril</th>
<th>difference</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GFR</td>
<td>-17.9</td>
<td>-14.9</td>
<td>3 ml/min</td>
<td>NS</td>
</tr>
<tr>
<td>SCr change</td>
<td>0.1</td>
<td>0.1</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Urine albumin excretion</td>
<td>1.03</td>
<td>0.99</td>
<td>1.04</td>
<td>NS</td>
</tr>
<tr>
<td>BP</td>
<td>145/80</td>
<td>147/83</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Adverse Events</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strokes</td>
<td>6 cases</td>
<td>6 cases</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>HF</td>
<td>9 cases</td>
<td>7 cases</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>nonfatal MI</td>
<td>9 cases</td>
<td>6 cases</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Deaths</td>
<td>6 cases</td>
<td>6 cases</td>
<td></td>
<td>NS</td>
</tr>
</tbody>
</table>

3. Will the results help me?
   * ~90% received the higher doses
   * high drop out rate (30%) mainly due to adverse events
   * The application of this trial to patients is limited because these patients had a history of diabetes for 8 years with very little renal insufficiency to begin with.

Conclusion: The DETAIL trial is one of few head-to-head comparison of ACEI’s and ARB’s on renal outcomes. This trial is diseased oriented and NOT patient-oriented. Therefore the data should not result in a change of practice. I think it does confirm again that ACEI can be used over ARBs to save money and be assured of similar results.