Combination ACE inhibitor and angiotensin-receptor blocker therapy was better than monotherapy in nondiabetic renal disease


**Question**
In patients with nondiabetic renal disease, what is the effectiveness of the angiotensin II–receptor blocker (ARB) losartan, the angiotensin-converting enzyme (ACE) inhibitor trandolapril, or the 2 drugs combined for delaying disease progression?

**Design**
Randomized (unclear allocation concealment*), blinded (clinicians, patients, data collectors, and monitoring committee),* controlled trial with 3-year follow-up.

**Setting**
Hospital outpatient renal clinic serving 3 cities in Japan.

**Patients**
301 patients 18 to 70 years of age who had chronic nondiabetic renal insufficiency, persistent proteinuria, and no history of allergic reaction to drugs. Exclusion criteria included immediate need for renal replacement therapy; need for corticosteroids, nonsteroidal antiinflammatory drugs, or immunosuppressive drugs; proteinuria > 10 g/d and hypoaalbuminemia < 28 g/L; other serious disease; and pregnancy or breastfeeding. 263 patients (mean age 45 y, 54% men) completed an 18-week run-in period and were randomized. Follow-up of these patients was 97%.

**Intervention**
Patients were allocated to losartan, 100 mg/d plus placebo (n = 89); trandolapril, 3 mg/d plus placebo (n = 86); or a combination of losartan, 100 mg, and trandolapril, 3 mg/d (n = 86).

**Main Outcome Measures**
A combined endpoint of time to doubling of serum creatinine level or end-stage renal disease (ESRD) (glomerular filtration rate < 7 mL/min per 1.73 m² or implementation of dialysis). Secondary outcomes were changes in blood pressure and urinary protein excretion, and adverse effects.

**Main Results**
Analysis was by intention to treat. At 3 years, fewer patients who received combination treatment reached the combined endpoint than did patients who received either drug with placebo (Table). Blood pressure did not differ between groups. Patients in the combination treatment group had the greatest decrease in urinary protein excretion rate (maximum decrease 75%) compared with losartan alone (42%) and trandolapril alone (44%). Groups did not differ for adverse effects, and no patient had an acute decline in renal function.

**Conclusion**
In patients with nondiabetic renal disease, losartan and trandolapril combined were better than either drug alone for delaying disease progression.


For correspondence: Dr. N. Nakao, Showa University, Yokohama, Japan. E-mail lancetjp@yahoo.co.jp.

*See Glossary.

### Combination therapy vs losartan or trandolapril alone for nondiabetic renal disease at 3 years†

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Comparisons</th>
<th>Event rates</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined endpoint</td>
<td>Combination therapy vs losartan</td>
<td>11% vs 23%</td>
<td>49% (0.5 to 75)</td>
<td>9 (5 to 1722)</td>
</tr>
<tr>
<td></td>
<td>Combination therapy vs trandolapril</td>
<td>11% vs 23%</td>
<td>50% (1.7 to 75)</td>
<td>9 (5 to 359)</td>
</tr>
</tbody>
</table>

†Combined endpoint = time to doubling of serum creatinine level or end-stage renal disease. Abbreviations defined in Glossary, RRR, NNT, and CI calculated from data in article.