Increasing evidence suggests that elevated cholesterol levels in mid-life are associated with increased risk of No patients had persistent elevations in creatine phosphokinase values. In this pre-planned, post hoc analysis of the population of genotyped patients, compared with placebo, atorvastatin Overall, 8 out of the 97 centers did not collect samples for genotyping. Approximately half of the non-genotyped The main LEADe study showed no significant differences between the treatment groups for the co-primary end Co-therapy with donepezil plus high-dose atorvastatin was well tolerated in patients with mild-to-moderate AD. Of 641 patients randomized in the 72-week double-blind treatment phase of LEADe, 514 subjects consented to Because some centers did not perform genotyping, the significant treatment effect observed in the genotyped group All patients had to have been receiving donepezil 10 mg for at least 3 months prior to screening. At study entry, subjects had to have low-density lipoprotein cholesterol (LDL-C) levels of 95–195 mg/dL. Exploratory analyses suggest that for change in AD Assessment Scale-cognitive subscale (ADAS-cog) and AD cooperative study-cognitive scale (ADCS-CGIC) scores, a significant effect on change in ADAS-cog score (P = 0.04), where higher baseline MMSE scores predicted a smaller decline in cognition, regardless }

<table>
<thead>
<tr>
<th>Table 4:</th>
<th><strong>Atorvastatin 80 mg + donepezil 10 mg</strong></th>
<th><strong>New genotyped</strong></th>
<th><strong>Non新颁布</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>AVG</strong></td>
<td><strong>SEM</strong></td>
<td><strong>AVG</strong></td>
</tr>
<tr>
<td>12-month change in ADAS-cog</td>
<td>-2.70 (0.36)</td>
<td>3.13 (0.60)</td>
<td>2.70 (0.36)</td>
</tr>
<tr>
<td>18-month change in ADAS-cog</td>
<td>-3.25 (0.41)</td>
<td>3.67 (0.64)</td>
<td>3.25 (0.41)</td>
</tr>
</tbody>
</table>

**Safety**

In the overall MITT population, 60 patients (18.1%) in the placebo plus donepezil 10 mg group experienced serious adverse events, compared with 67 patients (20.6%) in the placebo plus donepezil 10 mg group. Conclusion: Although the study was not powered to demonstrate differences in the incidence of serious adverse events, there was no evidence of a difference in the incidence of serious adverse events between the treatment groups. No patients had persistent elevations in creatine phosphokinase levels.

**SUMMARY**

The primary analysis of the LEADe study showed that in patients receiving background donepezil therapy, co-therapy with high-dose atorvastatin was associated with a significant reduction in the risk of deterioration compared with placebo. Combining atorvastatin and donepezil was associated with a significant benefit on the primary end point of change in ADAS-cog score. However, a post hoc analysis of the effect of NOS3 genotyping on treatment outcome suggested that the effect of atorvastatin on the primary end point was influenced by the NOS3 genotype. This observation raises questions about the role of genetic factors in the modulation of the therapeutic effects of atorvastatin in Alzheimer's disease. Further studies are needed to investigate the impact of genetic factors on the efficacy of atorvastatin in Alzheimer's disease.