Ezetimibe added to ongoing statin therapy reduced LDL cholesterol in primary hypercholesterolemia


**Question**
In patients with primary hypercholesterolemia not meeting cholesterol-lowering goals with dietary alteration and statin monotherapy, does the addition of ezetimibe to statin therapy reduce low-density lipoprotein cholesterol (LDL-C) levels more than placebo added to statin?

**Design**
Randomized [allocation concealed]*†, blinded (patients, clinicians, [data collectors, and data analysts]*) ‡, placebo-controlled trial with 8-week follow-up.

**Setting**
80 centers in the United States, Australia, Belgium, Canada, Denmark, Germany, Portugal, Spain, and Switzerland.

**Patients**
769 patients (mean age 60 y, 58% men) who had primary hypercholesterolemia, taking a stable dose of a statin for ≥6 weeks, and had received instruction on a cholesterol-lowering diet. Patients’ mean LDL-C level had to be at or above the recommended target level for their risk category defined by the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP) II guidelines. Exclusion criteria included cardiovascular events in the previous 3 months, uncontrolled endocrine or metabolic disease, and impaired renal or hepatic function. Follow-up was 95%.

**Intervention**
Patients were stratified by severity of hypercholesterolemia at screening (<18% and ≥18% above target LDL-C level), and allocated to ezetimibe, 10 mg/d (n = 379), or placebo (n = 390) while continuing ongoing, open-label statin therapy for 8 weeks.

**Main Outcome Measures**
Mean percentage change in baseline in LDL-C level. The proportion of patients who achieved NCEP ATP II target levels for LDL-C and adverse events were also assessed.

**Main Results**
Analysis was by intention to treat. The addition of ezetimibe to statin therapy led to a greater reduction in LDL-C level than did placebo (Table). The effectiveness of ezetimibe was not affected by type of statin used.

**Conclusion**
In patients with primary hypercholesterolemia, the addition of ezetimibe to statin therapy was more effective than placebo added to statin in reducing low-density lipoprotein cholesterol levels.

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*See Glossary.
†Information provided by author.

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<thead>
<tr>
<th>Outcome</th>
<th>Ezetimibe</th>
<th>Placebo</th>
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<tr>
<td>LDL cholesterol level (mmol/L)</td>
<td>Baseline</td>
<td>Mean percent change</td>
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<td>LDL = low-density lipoprotein.</td>
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<td>3.6</td>
<td>−25%</td>
<td>3.6</td>
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Several questions remain. Will the addition of ezetimibe to a low or moderate statin dose bring greater LDL-C reductions than high-dose statins in primary hypercholesterolemia? Will the apparent hepatic and musculoskeletal safety at 12 weeks of combined therapy endure over the long-term? Will ezetimibe yield the same reduction in clinical events seen with statins?

This, and other studies thus far, suggest that ezetimibe is a safe, effective, and complementary treatment option for patients with hypercholesterolemia. Until more data arrive, I will use it in my practice when patients do not tolerate statins or cannot achieve treatment goals despite moderate-to-high statin doses and an effective dietary program.

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**References**