Does ezetimibe modify clinical outcomes?

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Clinical question

Does ezetimibe modify clinical outcomes?

Bottom line

Only the IMPROVE-IT trial provides meaningful data on ezetimibe. In patients with acute coronary syndrome, adding ezetimibe to moderate-intensity statin therapy prevents 1 cardiovascular event for every 50 people treated for 7 years. Baseline low-density lipoprotein (LDL) level does not influence this benefit. There are no data for ezetimibe in primary prevention, but the benefit is likely lower proportional to baseline cardiovascular disease (CVD) risk.

Evidence

Several RCTs examine outcomes for 10 mg of ezetimibe or placebo added to statin therapy.

- IMPROVE-IT[1-3]: In 18144 patients with acute coronary syndrome (within 10 days) and LDL levels of 1.3 to 3.2 mmol/L, ezetimibe lowered LDL levels by 0.43 mmol/L (24%) at 1 year.
  -Clinical outcomes at 7 years included no difference in mortality (15.4% vs 15.3%) and significantly reduced CVD (32.7% vs 34.7%, NNT = 50, *P* = .016), myocardial infarction (NNT = 59, *P* = .002), and ischemic stroke (NNT = 167, *P* = .008).
    —Benefits were seen regardless of baseline LDL level.
    —There were no differences in adverse events.
- ENHANCE[4]: In 720 patients with familial hypercholesterolemia, there was no difference in events at 2 years.
- Vascular surgery patients[5]: In 262 patients there was no difference in events at 1 year.

One RCT (N = 363) comparing ezetimibe and niacin (only other active comparator trial)[6] found significantly increased CVD events with ezetimibe (5% vs 1%, *P* = .04) at 14 months.

Context

- Two RCTs examine statin therapy plus ezetimibe versus placebo in which the effects of ezetimibe and statin therapy cannot be separated.
  -SEAS[7]: In 1873 aortic stenosis patients, there was no difference in composite valvular or ischemic CVD events.
  -SHARP[8]: In 9270 chronic kidney disease patients (one-third receiving dialysis), there was significantly reduced CVD (11.3% vs 13.4%, NNT = 48, *P* = .002).
- There are no primary prevention data for ezetimibe. If the relative effects are generalizable (as they are for statins[9]), for patients receiving low or moderate intensity statin therapy (eg, 20-40 mg of simvastatin or 10 mg of atorvastatin) the following would be expected:
  -Adding ezetimibe would prevent 1 CVD event in approximately 100 high-risk patients (20% baseline 10-year CVD risk) and approximately 200 low-risk patients (10% baseline 10-year CVD risk).[1-3]
  -Increasing to a high-intensity statin (eg, 80 mg of atorvastatin) would prevent 1 CVD event in approximately 43 high-risk and approximately 85 low-risk patients.[9]

Implementation

In patients with CVD who tolerate a low- to moderate-dose statin, 2 evidence-based lipid-lowering interventions further decrease CVD events: increasing to a high-dose statin or adding ezetimibe. Increasing to a high-dose statin is more than twice as effective as adding ezetimibe. High-dose statins cause intolerable adverse effects for 1 in about 50 patients and diabetes in 1 in about 125 patients over 5 years[10,11]; adding ezetimibe does not increase adverse effects.[1-3] Finally, 10 mg of atorvastatin plus ezetimibe costs $240 every 90 days versus $50 for 80 mg of atorvastatin.[12]

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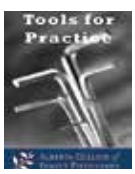

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