**Ezetimibe lowers LDL cholesterol, but what else?**

**Clinical Question:** Does ezetimibe modify clinical outcomes?

**Bottom-Line:** Only the IMPROVE-IT trial provides meaningful data on ezetimibe. In acute coronary syndrome patients, adding ezetimibe to moderate-intensity statin prevents one cardiovascular event for every 50 people treated for seven years. Baseline LDL level did not influence this benefit. There are no data for ezetimibe in primary prevention, but the benefit is likely proportional to (lower) baseline CVD risk.

**Evidence:**
- Randomized controlled trials (RCTs) of ezetimibe 10 mg or placebo added to statin:
  - IMPROVE-IT:1-3 18,144 patients with acute coronary syndrome (within 10 days) and LDL 1.3-3.2 mmol/L.
    - Ezetimibe lowered LDL by 0.43 mmol/L (24%) at one year.
    - Clinical outcomes at seven years:
      - Mortality: No difference (15.4% vs 15.3%).
      - Significantly reduced cardiovascular disease (CVD): 32.7% vs 34.7%, number needed to treat (NNT)=50.
      - Significantly reduced myocardial infarction (NNT=59) and ischemic stroke (NNT=167).
      - Note: Benefit seen regardless of baseline LDL level.
      - No difference in adverse events, including cancer, gastrointestinal, and musculoskeletal.
- ENHANCE: 720 patients with familial hypercholesterolemia. No difference in events at two years.
- 262 vascular surgery patients: No difference in events at one year.
- RCT of 363 patients comparing ezetimibe versus niacin (only other active comparator trial):
  - Significantly increased CVD events with ezetimibe (5% vs 1%) at 14 months.

**Context:**
- Two RCTs of statin plus ezetimibe versus placebo in which effect of ezetimibe and statin cannot be separated:
  - SEAS: 1,873 aortic stenosis patients: No difference in composite valvular/ischemic CVD events.
  - SHARP: 9,270 chronic kidney disease patients (⅓ on dialysis): Significantly reduced CVD 11.3% vs 13.4% (NNT=48).
- No primary prevention data for ezetimibe. If the relative effects are generalizable (as they are for statins), for patients receiving low-moderate intensity statin (e.g. simvastatin 20-40 mg or atorvastatin 10 mg):
  - Adding ezetimibe would prevent one CVD event in:
    - ~100 high-risk patients (20% baseline 10-year CVD risk).
    - ~200 low-risk patients (10% baseline 10-year CVD risk).
  - Whereas increasing to high-intensity statin (e.g. atorvastatin 80 mg) would prevent one CVD event in:
    - ~43 high-risk patients.
    - ~85 low-risk patients.

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