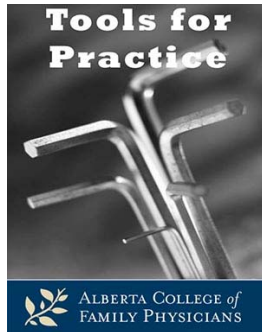


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Ezetimibe:

Lowers LDL cholesterol but what else?

Clinical Question:

Does Ezetimibe (Ezetrol) modify clinical outcomes?

Evidence:

Two Randomized Controlled Trials (RCT) assessed carotid intimal thickness as a surrogate of cardiovascular disease (CVD).^{1,2} Both used statins equally in both arms of the trial.

- RCT¹, 720 hypercholesterolemia patients, Ezetimibe 10mg or placebo
 - Ezetimibe: LDL decreased 1.3 mmol/L more
 - No difference in carotid intima thickness (plaque)
 - CVD events: Ezetimibe 10 vs placebo 7 (not statistically different)
- RCT², 363 patients, 77% had CVD, Ezetimibe 10mg or Niacin titrated to 2000mg
 - Carotid intimal thickness
 - Ezetimibe ↓ 0.0007 mm vs Niacin ↓ 0.0142 mm (20 times better)
 - CVD events: 5% Ezetimibe vs 1% Niacin (statistically significant), Number Needed to Treat (NNT) 24 for Niacin over Ezetimibe

Context:

- "SEAS" randomized 1873 calcific aortic stenosis patients to simvastatin 40mg + ezetimibe 10mg or Placebo.³
 - By combining statin and ezetimibe vs placebo we can't determine ezetimibes' contribution.
 - Treatment led to no difference in the primary composite outcome but statistically significant:
 - 54% LDL reduction
 - Fewer CABG (3.5%, NNT 29)
 - More cancer deaths (1.6%, NNH 63)
- Cancer data from 2 ongoing ezetimibe trials (SHARP & IMPROVE-IT):⁴
 - A non-significant increase in cancer deaths in both trials
 - Three studies combined: statistically more cancer deaths (+0.2%/year; NNH

108 over 5 years)

- While LDL reduction theory seems to apply to most statins trials, examples exist where changes in lipids have not produced clinical advantages.
 - Torcetrapib reduced LDL 25% and raised HDL 72% but increased CVD (NNH 84) and mortality (NNH 222).⁵ The medicine was withdrawn.

Bottom-line: Eight years after being licensed by the FDA, there is still no evidence that ezetimibe reduces cardiovascular outcomes. It may be worse than niacin and there is concern about a potential increased cancer mortality risk.

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1. [N Engl J Med 2008;358:1431-43.](#)
2. [N Engl J Med 2009;361:2113-22.](#)
3. [N Engl J Med 2008;359:1343-56.](#)
4. [N Engl J Med 2008;359:1357-66.](#)
5. [N Engl J Med 2007;357:2109-22.](#)

Tools for Practice is a biweekly article summarizing medical evidence with a focus on topical issues and practice modifying information. It is coordinated by G. Michael Allan, MD, CCFP and the content is written by practising family physicians. Archived articles are available on the Toward Optimized Practice and ACFP websites.

This communication reflects the opinion of the author and does not necessarily mirror the perspective and policy of the Alberta College of Family Physicians.