Status Of Cholesterol Lowering Drug Zetia (Ezetimibe) And Its Combination With Statins (Vytorin): Do They Help To Prevent Cardiovascular Events More Than Statins Alone: Who Should Be On Them: The IMPROVE-IT Trial

Don Poldermans

No Target and Statins Only?

How Low Is Low Enough?

2013 ACC/AHA Cholesterol Guidelines

restricted to placebo-controlled randomised trials with outcome data

1. No LDL-C goals

   No requirements to measure LDL-C levels or to attain specific LDL-C goal.

   ... given the absence of data on titration of drug therapy to specific goals, no recommendations are made for or against specific LDL-C goals...

   "Fire and Forget Using Fixed Statin Regimens"

2. No value for drugs other than statins

Fewer options for combinations of lipid lowering therapy.

... in patients with insufficient response to statins ... one might consider the use of a non-statin cholesterol lowering therapy ... preferentially from randomized clinical trials

"No clear place for ezetimibe"

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"No clear place for ezetimibe"
IMPROVE-IT vs. CTT: Ezetimibe vs. Statin Benefit


**CHD death**
**Coronary Death**
**Major coronary events (nfMI + CHD)**
**Non-fatal MI**
**Major vascular events (MCE+CR+stroke)**
**Any stroke**
**Ischemic stroke**

### CTT HR per 1mM LDL-C Reduction for 26 Statin Trials

**Conclusion:** “…each 1.0 mmol/L reduction reducing the annual rate of (these) major vascular events by just over a fifth”

### Safety Events

- Myalgia /CK AE
- Discon AST or ALT >3x
- Gall bladder AE
- Neurocognitive

### Impact of dual lipid-lowering strategy with atorvastatine and ezetimibe on coronary plaque regression (n = 202)

- LDL-C: 63 vs 73 mg/dL
- Percent atheroma volume change: 78% vs 58%; p = 0.004

L = lipitor // LZ = lipitor + ezetimibe
Follow-up: 9-12 months

**Take home message**

**IMPROVE-IT:** First trial demonstrating incremental clinical benefit when adding a non-statin agent (ezetimibe) to statin therapy:

- **YES:** Non-statin lowering LDL-C with ezetimibe reduces cardiovascular events
- **YES:** Even Lower is Even Better (achieved mean LDL-C 53 vs. 70 mg/dL at 1 year)
- **YES:** Confirms ezetimibe safety profile

Comparison with CTT data suggest the treatment effect per 1mM reduction of LDL-C associated with adding ezetimibe to a statin is consistent with that achieved per 1mM of LDL-C reduction with statins.