High dose atorvastatin was superior to standard dose pravastatin in reducing death or major CV events in acute coronary syndrome


Clinical impact ratings GP/FP/Primary care ★★★★★☆ IM/Ambulatory care ★★★★★☆ Internal medicine ★★★★★☆ Cardiology ★★★★★☆

In patients with an acute coronary syndrome (ACS), is standard dose pravastatin non-inferior to high dose atorvastatin for reducing death or major cardiovascular (CV) events?

METHODS

**Design:** randomised, placebo controlled trial (Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction 22 [PROVE-IT TIMI 22] trial).

**Allocation:** concealed. *

**Blinding:** blinded (clinicians and patients). *

**Follow up period:** mean 24 months.

**Setting:** 349 sites in 8 countries.

**Patients:** 4162 stable patients (mean age 58 yr, 78% men) who were hospitalised for an ACS in the previous 10 days, were enrolled after a percutaneous revascularisation procedure (if planned), and had a total cholesterol concentration < 240 mg/dl (6.21 mmol/l) taken within the first 24 hours, or < 6 months after the onset of the ACS. Exclusion criteria included shortened expected survival to < 2 years and daily statin use.

**Intervention:** daily standard dose pravastatin (40 mg) (n = 2063) or high dose atorvastatin (80 mg) (n = 2099).

**Outcomes:** composite of major CV events: all cause death, myocardial infarction (MI), unstable angina requiring hospital readmission, revascularisation (> 30 d after randomisation), and stroke. Secondary outcomes included coronary heart disease (CHD) death, revascularisation, and non-fatal MI.

**Patient follow up:** 99.8% (intention to treat analysis).

*See glossary.

MAIN RESULTS

Atorvastatin led to greater reductions in the composite endpoint: death caused by CHD, non-fatal MI, or revascularisation; revascularisation alone; or unstable angina requiring hospital admission than did pravastatin (table). The upper limit of the CI exceeded the prespecified boundary (< 1.17) for showing equivalence. Groups did not differ for all cause death (p = 0.07), death or MI (p = 0.06), stroke, or adverse effects (p = 0.11).

CONCLUSION

In patients with an acute coronary syndrome, standard dose pravastatin was inferior to high dose atorvastatin in reducing death or major cardiovascular events.

Abstract and commentary also appear in ACP Journal Club.

**Commentary**

The study by Cannon et al shows that more intensive lowering of low density lipoprotein (LDL) cholesterol with statin treatment in patients with a recent ACS reduced subsequent risk of major adverse CV events. This trial also supports the hypothesis that more aggressive LDL reduction to target concentrations of 60 mg/dl (1.5 mmol/l) yields greater benefit than the current guideline recommendation (LDL concentrations < 100 mg/dl [2.6 mmol/l]).

In the ACS population, the benefit of very aggressive LDL reduction compared with moderate reduction is evident as early as 1 month after initiating therapy. This reduction would take 2 years in patients with stable coronary artery disease. In the MIRACL study, high dose atorvastatin therapy initiated within days of an ACS diagnosis reduced recurrent ischaemic events within 16 weeks. Early, aggressive statin therapy in patients with ACS has a powerful role in "passivating" the unstable and vulnerable plaque(s).

The subgroup analysis in the study by Cannon et al showed a less prominent benefit in patients with lower baseline LDL concentrations and previous statin therapy. The results fell between those of the CARE trial in which a lack of benefit was observed in patients with baseline LDL concentrations < 125 mg/dl (3.2 mmol/l) and those of the Heart Protection Study in which a consistent benefit was observed regardless of baseline LDL concentrations. Patients with lower baseline LDL concentrations or previous statin treatment would be expected to accrue less absolute benefit because they have a lower baseline risk. Therefore, current practice recommendations for patients with ACS should include obtaining a lipid and liver profile on hospital admission, and initiating or intensifying statin therapy to achieve target LDL concentrations < 70 mg/dl (1.8 mmol/l), if no contraindication exists.

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