THERAPEUTICS

Fluvastatin reduced major adverse cardiac outcomes after first percutaneous coronary intervention

Serruys PW, de Feyter P, Macaya C, et al., for the Lescol Intervention Prevention Study (LIPS) Investigators. **Fluvastatin for prevention of cardiac events following successful first percutaneous coronary intervention: a randomized controlled trial.** JAMA. 2002;287:3215-22.

QUESTION

In patients having percutaneous coronary intervention (PCI), does cholesterol lowering with fluvastatin prevent major adverse cardiac events (MACEs) more than placebo?

DESIGN

Randomized (unclear allocation concealment*), blinded (clinicians, patients, and outcome assessors),* placebo-controlled trial with mean 3.9-year follow-up.

SETTING

77 centers in 10 countries.

PATIENTS

1677 patients 18 to 80 years of age (mean age 60 y, 84% men) who had completed a first PCI and had total cholesterol levels 3.5 to 7.0 mmol/L and fasting triglyceride levels < 4.5 mmol/L before the index procedure. Exclusion criteria were high blood pressure uncontrolled with treatment, left ventricular ejection fraction < 30%, previous PCI or coronary artery bypass grafting (CABG), severe valvular or renal disease, idiopathic cardiomyopathy or congenital heart disease, obesity, or malignant or other disease associated with a life expectancy < 4 years. All patients were included in the intention-to-treat analysis.

INTERVENTION

Patients were allocated to fluvastatin, 40 mg twice per day (Lescol, Novartis Pharma, Basel, Switzerland) (n = 844) or placebo (n = 833) for 3 to 4 years. If total cholesterol exceeded 7.2 mmol/L for ≥ 3 months, patients discontinued study medication and received an open-label cholesterol-lowering therapy.

MAIN OUTCOME MEASURES

The primary outcome was a composite end point (development of a MACE) defined as cardiac death, nonfatal myocardial infarction (MI), or a reintervention (CABG, repeated PCI, or PCI for a new lesion).

MAIN RESULTS

Analysis was by intention to treat. During follow-up, fewer patients who received fluvastatin had ≥ 1 MACE than did patients who received placebo (Table). MACE-free survival time was longer in the fluvastatin group than in the placebo group (first quartile of time to first MACE 1558 vs 1227 d, P = 0.01).

CONCLUSION

In patients having percutaneous coronary intervention, cholesterol lowering with fluvastatin reduced major adverse cardiac events more than placebo.

Source of funding: Novartis Pharma AG.

For correspondence: Dr. P.W. Serruys, Academic Hospital, Rotterdam, The Netherlands. E-mail serruys@card.azr.nl.

*See Glossary.

Fluvastatin vs placebo to prevent a major adverse coronary event (MACE) after percutaneous coronary intervention at a mean of 3.9 years†

Outcome	Fluvastatin	Placebo	RRR (95% CI)	NNT (CI)
≥ 1 MACE	21.4%	26.7%	20% (4.5 to 32)	20 (11 to 90)

†Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

PCI has become the preeminent procedure to reduce atherosclerotic obstruction of coronary arteries and consequently improve patient symptoms as well as lessen the risk for subsequent vascular ischemic events. However, PCI has 2 major limitations: acute ischemic complications (mostly MI and urgent repeated intervention) and late restenosis. Recent investigations also suggest that coronary atherosclerosis is a diffuse inflammatory disease. Thus, even in the setting of an acute unstable event, treatments are needed that address the systemic nature of the process and not just the focal "culprit" lesions (1).

The study by Serruys and colleagues adds important findings on the use of the statin class of lipid-lowering drugs among patients at risk for, or with, vascular disease. It extends the clinical benefits of this class of drugs to fluvastatin and, along with the recently reported Heart Protection Study (2), shows that the effects of statin treatment are consistent regardless of baseline lipid levels. This latter observation suggests that benefits from statin treatment are not solely attributable to lipid lowering. This evidence shows the merit of treating vascular disease as a systemic inflammatory state (3), coupling focal treatments such as PCI with aggressive medical therapy (now including antiplatelet drugs and angiotensin-converting enzyme inhibitors in addition to statins).

Little doubt now exists that most patients at high risk for vascular disease, and certainly all with proven disease, should have a statin drug prescribed as a key part of their long-term medical regimen. Ongoing trials will provide information regarding the relative value of the aggressiveness of lipid-lowering, will compare various statins, and will determine whether new agents might improve safety while maintaining efficacy.

Robert A. Harrington, MD
Duke University Medical Center
Durham, North Carolina, USA

References

1. **Buffon A, Biasucci LM, Liuzzo G, et al.** Widespread coronary inflammation in unstable angina. N Engl J Med. 2002;347:5-12.
2. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet. 2002;360:7-22.
3. **Bhatt DL, Topol EJ.** Need to test the arterial inflammation hypothesis. Circulation. 2002;106:136-40.

