

Adding ezetimibe to atorvastatin improves lipid control

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Adding ezetimibe to atorvastatin significantly boosted the attainment of lipid targets as specified by both Canadian and European guidelines in elderly patients aged 65 and older and the combination produced superior results than simply increasing the dose of atorvastatin alone, Dr. Christian Constance told the Canadian Cardiovascular Congress 2009, co-hosted by the Heart and Stroke Foundation and the Canadian Cardiovascular Society.

"The population of people age 65 and older is growing but very few studies have looked at the efficacy of lipid-lowering drugs in this group of patients. We wanted to see whether adding ezetimibe to atorvastatin would be as effective as doubling or even quadrupling the dose of atorvastatin in this age group," said Dr. Constance, of the University of Montreal.

The study included 2,055 patients who were at high risk for [coronary heart disease](#) or who had been diagnosed with arterial vascular disease and who were not at the following cholesterol targets:

- Less than 2 mmol/L for low density lipoprotein cholesterol (LDL-C)
- Less than 4 mmol/L for total cholesterol (TC)
- TC to high density lipoprotein cholesterol (HDL) ratio less than 4
- Less than 0.85g/L for apolipoprotein B (ApoB)
- Less than 1.0 mg/L for high sensitivity-C-reactive protein (hs-CRP)

The patients were stabilized on atorvastatin 10 mg/day for six weeks and then were randomized to receive either ezetimibe 10 mg/day in addition to

atorvastatin 10 mg/day for 12 weeks or to atorvastatin 20 mg/day for six weeks, followed by a quadrupling of atorvastatin to 40 mg/day for six weeks.

Significantly more patients achieved their lipid targets with the ezetimibe plus atorvastatin combination compared with double or quadruple dose monotherapy with atorvastatin. For example, the percent of patients achieving their LDL-C targets on the ezetimibe/atorvastatin combination at 12 weeks was 60.5% compared with 49.7% for patients on the atorvastatin 20mg/40mg regimen [Odds ratio (95% CI)1.55 (1.21, 1.98)].

All treatments were well tolerated.

"Whether you look at European LDL targets or Canadian LDL targets, we reached LDL targets much easier with the combination ezetimibe atorvastatin 10 mg. than even atorvastatin 40 mg. The European guidelines are a little more strict," Dr. Constance said.

"It's a numbers game," he added. "The more you get to those targets, the less patients will have events. And the lower dose of statin, the better it is tolerated, especially in the older, high risk patients, who were the subjects of this study."

The differences between the LDL-cholesterol levels that were achieved were quite striking, said Dr. Charles Kerr, president of the Canadian Cardiovascular Society. "This is a very well-designed trial and the evidence is very convincing that adding ezetimibe to a lower dose of atorvastatin may be more effective than just increasing the dose. Essentially what we have been doing with the statin drugs is doubling them until we achieve goal."

Ezetimibe is a cholesterol lowering drug that acts differently from the statins, he added. "Ezetimibe blocks the absorption of cholesterol from the gut;

whereas statins alter metabolism in the liver. This study suggests that adding ezetimibe can be an effective way of reducing [cholesterol](#) perhaps more so than increasing the doses of statins."

Source: Heart and Stroke Foundation of Canada

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