

Letter to the Editor

Ezetimibe – a new approach in hypercholesterolemia management

Michael S. Kostapanos^{1,2}, Moses S. Elisaf², Dimitri P. Mikhailidis¹

Correspondence: Dimitri P. Mikhailidis, e-mail: mikhailidis@aol.com

Key words: ezetimibe, low density lipoprotein cholesterol, atherosclerosis, cardiovascular events

Suchy et al. [10] discuss the benefits of ezetimibe beyond lipid-lowering as well as its effects on atherosclerosis. Some comments may be of interest.

Reducing low density lipoprotein cholesterol (LDL-C) is the main indication for ezetimibe [2, 7, 8]. This drug is useful in patients who cannot achieve LDL-C goals on statins or those who are statin intolerant [2, 4, 7, 8]. Meta-analyses suggested that adding ezetimibe decreases LDL-C levels more than statin monotherapy, after doubling the dose of a statin or selecting a more potent statin [2, 7, 8]. It was also suggested that ezetimibe can increase LDL particle size, especially in patients with high triglyceride levels [3, 11].

Ezetimibe may exert other beneficial actions which may or may not be related to its hypolipidemic capacity (e.g., for non-alcoholic fatty liver disease and renoprotection) [6]. Ezetimibe monotherapy reduced the plasma mass and activity of lipoprotein-associated phospholipase A₂ (Lp-PLA₂), which is considered risk predictor of cardiovascular (CV) events [9]. Furthermore, ezetimibe may lower the levels of oxidative stress markers [5].

In the end, the most important issue is reducing vascular events. In this context, the Study of Heart and Renal Protection (SHARP) [1] reported that the combination of ezetimibe with simvastatin was associated with reduced risk of CV events compared with

placebo after 4.9 years in patients (n = 9,270) who are pre-dialysis or on dialysis.

The clinical relevance of these points and those addressed by Suchy et al. [10] requires to be established by future studies.

References:

- Baigent C, Landray MJ, Reith C, Emberson J, Wheeler DC, Tomson C, Wanner C et al. SHARP Investigators: The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial. Lancet, 2011, 377, 2181–2192.
- Catapano A, Brady WE, King TR, Palmisano J: Lipid altering-efficacy of ezetimibe co-administered with simvastatin compared with rosuvastatin: a meta-analysis of pooled data from 14 clinical trials. Curr Med Res Opin, 2005, 21, 1123–1130.
- Kalogirou M, Tsimihodimos V, Gazi I, Filippatos T, Saougos V, Tselepis AD, Mikhailidis DP et al.: Effect of ezetimibe monotherapy on the concentration of lipoprotein subfractions in patients with primary dyslipidaemia. Curr Med Res Opin, 2007, 23, 1169–1176.
- 4. Kostapanos MS, Athyros VG, Karagiannis A, Mikhailidis DP: Therapeutic options for statin-intolerant patients. Curr Med Res Opin, 2012, 28, 345–349.
- 5. Kostapanos MS, Spyrou AT, Tellis CC, Gazi IF, Tselepis AD, Elisaf M, Liberopoulos EN: Ezetimibe treatment

¹Department of Clinical Biochemistry, Royal Free Hospital campus, University College London, Medical School, University College London (UCL), UK

²Department of Internal Medicine, School of Medicine, University of Ioannina, Ioannina, Greece

- lowers indicators of oxidative stress in hypercholesterolemic subjects with high oxidative stress. Lipids, 2011, 46, 341–348.
- Lioudaki E, Ganotakis ES, Mikhailidis DP: Ezetimibe; more than a low density lipoprotein cholesterol lowering drug? An update after 4 years. Curr Vasc Pharmacol, 2011, 9, 62–86.
- Mikhailidis DP, Lawson RW, McCormick AL, Sibbring GC, Tershakovec AM, Davies GM, Tunceli K: Comparative efficacy of the addition of ezetimibe to statin vs statin titration in patients with hypercholesterolaemia: systematic review and meta-analysis. Curr Med Res Opin, 2011, 27, 1191–1210.
- 8. Mikhailidis DP, Sibbring GC, Ballantyne CM, Davies GM, Catapano AL: Meta-analysis of the cholesterol-

- lowering effect of ezetimibe added to ongoing statin therapy. Curr Med Res Opin, 2007, 23, 2009–2026.
- Saougos VG, Tambaki AP, Kalogirou M, Kostapanos M, Gazi IF, Wolfert RL, Elisaf M et al.: Differential effect of hypolipidemic drugs on lipoprotein-associated phospholipase A2. Arterioscler Thromb Vasc Biol, 2007, 27, 2236–2243
- Suchy D, Łabuzek K, Stadnicki A, Okopień B: Ezetimibe a new approach in hypercholesterolemia management. Pharmacol Rep, 2011, 63, 1335–1348.
- 11. Winkler K, Jacob S, Müller-Schewe T, Hoffmann MM, Konrad T: Ezetimibe alone and in combination lowers the concentration of small, dense low-density lipoproteins in type 2 diabetes mellitus. Atherosclerosis, 2012, 220, 189–193.