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Expert Opinion

Author's reply: Managing the combination of non-alcoholic fatty liver disease and metabolic syndrome

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We thank our colleagues for the timely letter, giving us the opportunity to underline a point which was not considered in our review [1], i.e., the tight control of cholesterol levels and cardiovascular risk by statins.

Several recent studies suggested that elevated liver enzymes (namely alanine aminotransferase and particularly γ-glutamyl-transpeptidase levels [2]) are significantly associated with cardiovascular risk, independent of established risk factors and the features of the metabolic syndrome. This evidence fits with the results of the GREACE study, where atorvastatin treatment in subjects with coronary disease and abnormal liver tests reduced both cardiovascular events and liver enzymes [3].

Unfortunately, when statins were used to reduce fatty liver, the results were disappointing. In a comprehensive meta-analysis, Musso *et al.* identified 4 RCT of statin use in NAFLD [4]. In the only study based on repeated liver biopsies, simvastatin did not improve histological outcomes; in the remaining studies atorvastatin improved the ultrasonographic imaging of the liver and/or liver enzymes, as biochemical markers of steatosis. In the large St. Francis Heart Study, atorvastatin combined with vitamin E and C significantly reduced the odds of NAFLD in a 3.6-year follow-up [5]. Ezetimibe was evaluated in 2 uncontrolled trials and 2 RCTs, consistently improving liver histology and plasma lipids [4]. Notably all studies reported that statins were well-tolerated [6], confirming the results of Chalasani *et al.* that patients with elevated liver enzymes are not at higher risk for statin hepatotoxicity [7].

Triglyceride accumulation in the liver should no longer be considered a mere epiphenomenon of the dyslipidemia associated with insulin resistance, but steatosis probably participates in the metabolic imbalance and drives an additional cardiovascular risk. A comprehensive management of NAFLD must include an effective drug treatment of hyperlipidemia to reduce both liver disease progression and cardiovascular-related outcomes, and statins may be a valuable opportunity.

Declaration of interest

G Marchesini has received honoraria from Sanofi and Roche. All other authors have nothing to declare.

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