Smoking and non-alcoholic steatohepatitis (NASH): The GREek Atorvastatin and Coronary heart disease Evaluation (GREACE) trial

To the Editor:

As the authors of the GREek Atorvastatin and Coronary heart disease Evaluation (GREACE) trial [1], we appreciate the comments made by Babu *et al.* [2] and Zein *et al.* [3] regarding the role of smoking on non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH). A few comments may be of interest.

First, we assessed changes in vascular risk and the safety of statins [1]. We could not analyse every possible relationship.

Second, in order to interpret the results of GREACE in terms of NAFLD/NASH, there is a need to know how many patients were smokers at the end of this trial. Essentially, the numbers were similar to baseline values.

Third, it would be interesting to know the transaminase status at the end of the GREACE study. In the NAFLD + not on statin group, alanine aminotransferase (ALT) activity in smokers (n = 19) was 70 ± 7 *vs.* 61 ± 9 U/L in non-smokers (n = 191), p <0.0001. Therefore, smokers maintained a raised ALT activity over the 3-year duration of the trial. In the NAFLD + on statin group, ALT activity in smokers (n = 23) was 37 ± 6 *vs.* 37 ± 5 U/L in non-smokers (n = 204), p = 0.10. This suggests that statins improved ALT activity in smokers. These findings are limited because they are based on a *post hoc* analysis and the number of patients is small.

Our findings support the hypothesis discussed by Babu *et al.* [2] and Zein *et al.* [3] regarding the adverse effect of smoking on NAFLD and NASH. More work is needed in this field.

Conflict of interest

This letter was written independently. The authors did not receive financial or professional help with the preparation of the manuscript. DPM has given talks, attended conferences, and participated in advisory boards and trials sponsored by various pharmaceutical companies (MSD, Genzyme, and Abbott).

References

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Dosage-sensitive network in polycystic kidney and liver disease: Multiple mutations cause severe hepatic and neurological complications

To the Editor:

Single kidney and liver cysts are common. If cysts occur multiply and earlier in life, they are mostly inherited. Autosomal dominant polycystic kidney disease (ADPKD) is one of the most common genetic disorders with mutations in *PKD1* or *PKD2* and affects 10–15 million individuals worldwide [1]. Variable disease expression even in the same family is incompletely understood, some have intracranial aneurysms and most elderly patients show liver cysts. Polycystic liver disease (ADPLD) is caused by a dominant mutation in *PRKCSH* or *SEC63*, involved in posttranslational translocation and quality control of proteins (such as the ADPKD proteins) [2]. ADPLD patients can also harbour kidney cysts. Morphologically, cysts are indistinguishable from those in ADPKD. In mice, both diseases overlap not only clinically, but also genetically and functionally, in line with a dosage-sensitive network for polycystic liver and kidney disease [3].

We describe a family with liver and kidney cysts in which the much more severely affected 39-year-old index patient (Fig. 1, arrow) harbours a total of four mutant alleles in genes for PKD and PLD, suggesting a dosage effect that may explain her severe phenotype. Three aneurysms of the right middle cerebral artery (MCA) led to subarachnoid haemorrhage at the age of 38 and were surgically clipped. In addition, dissections of both carotid arteries led to right-sided stenosis (Fig. 1). Massive liver disease