New Hope for Chronic Kidney Disease Patients After the JUPITER Trial

Myth or Reality?

In their recent paper, Ridker et al. (1) performed a secondary analysis of JUPITER (Justification for the Use of Statins in Prevention–an Intervention Trial Evaluating Rosuvastatin) to assess the efficacy of rosuvastatin in primary prevention in patients with moderate chronic kidney disease (CKD). According to their results, rosuvastatin reduces first cardiovascular events and all-cause mortality among men and women with low-density lipoprotein cholesterol <130 mg/dl, elevated high-sensitivity C-reactive protein, and moderate CKD (estimated glomerular filtration rate <60 ml/min/1.73 m²).

The authors’ results are in accordance with previous secondary/post hoc analyses of major secondary prevention statin trials. In particular, the HPS (Heart Protection Study) (2), the CARE (Cholesterol And Recurrent Events) study (3), and the Pravastatin Pooling Project (4) suggested a beneficial effect of statins on cardiovascular end points. Conversely, both the PREVENT IT (Prevention of Renal and Vascular End Stage Disease Intervention Trial) (5)—the only prospective randomized trial evaluating the role of statins in patients with mild CKD—and ALERT (Assessment of Lescol in Renal Transplant Trial) (6) failed to detect any cardiovascular benefit of statins in nondialysis CKD patients. To further complicate things, a recent meta-analysis involving 25,017 pre-dialysis patients concluded that statins significantly reduced the all-cause and cardiovascular mortality (7).

The results of this secondary analysis of the JUPITER trial should be interpreted with caution for the following reasons. First, the JUPITER trial enrolled patients without overt diabetes mellitus, in contrast to the 4D (Die Deutsche Diabetes Dialyse) study, which employed diabetic dialysis patients (8). Moreover, in AURORA (A Study to Evaluate the Use of Rosuvastatin in Subjects on Regular Hemodialysis: An Assessment of Survival and Cardiovascular Events), there was an almost statistically significant predominance of patients with diabetes or diabetic nephropathy as the cause of end-stage renal disease in the statin group (9). Because diabetes is an independent cardiovascular risk factor, statins might not confer any benefit in terms of primary prevention in diabetic CKD patients. Second, of 3,267 patients included in the study, only 14 had stage IV CKD. It is well established that cardiovascular mortality increases progressively through the stages of CKD (10), and thus it might be too late for statins to provide any benefit in stage IV to V CKD patients. Therefore, the findings of this analysis cannot be extrapolated to patients with CKD and diabetes or beyond stage III CKD.

Regarding the effects of statins on renal function, the present study did not detect a significant difference in the change of estimated glomerular filtration rate between the rosuvastatin and the placebo arms after 1 year of follow-up. However, the follow-up was short, and again, this study enrolled almost only a specific subgroup of CKD patients (stage III CKD). It should be noted that data from secondary/post hoc analyses of the major statin trials are more robust in supporting a renoprotective effect of statins in CKD patients compared with their cardioprotective effects (11), whereas 2 recent large meta-analyses did not show an impact of statins on glomerular filtration rate (7,12).

Given the conflicting findings on the cardioprotective and renoprotective role of statins along with their potentially harmful effects (13), the results of SHARP (Study of Heart and Renal Protection) (14) and PLANET (Prospective Evaluation of Proteinuria and Renal Function in Diabetic Patients With Progressive Renal Disease Trial) (15) are eagerly anticipated.

References