Dear Sir,

Bezafibrate is a lipid-lowering agent [1] used for the treatment of dyslipidaemia associated with diabetes mellitus [2]. It has also been shown to worsen renal function in subjects with chronic renal failure [3] or renal transplant recipients [4]. To determine whether bezafibrate is appropriate for use in diabetic subjects with mild renal impairment (creatinine < 145 µmol·l\(^{-1}\)), we studied 24 subjects with nephropathy associated with type 2 diabetes mellitus. Twenty-four subjects with mild renal impairment (estimated GFR at baseline 91 ± 49 ml·min\(^{-1}\)·1.73m\(^{2}\)) and dyslipidaemia (cholesterol > 6.2 mmol·l\(^{-1}\), triglycerides > 2.3 mmol·l\(^{-1}\) and HDL cholesterol < 0.9 mmol·l\(^{-1}\)) were randomised to receive either slow release bezafibrate (Bezalip Retard, Boehringer Mannheim) 400 mg daily or placebo for 6 months in a double-blind design (n = 12 in each group). Subjects had either stable, controlled blood pressure on anti-hypertensives for 6 months (n = 8 in placebo group, n = 9 in bezafibrate group) or were not hypertensive (BP < 160/90). Non-diabetic renal disease was excluded on clinical grounds, absence of urinary infection or active urinary sediment.

Subjects were similar in both groups in terms of age (mean 58 ± 9 years for whole group), BMI, smoking, years since diagnosis of diabetes, glycaemic control, protein intake (determined indirectly by 24-hour urinary urea excretion) and blood pressure throughout the 6-month study. During a 6-week run-in period on a low fat diet, cholesterol concentrations decreased from 7.2 ± 1.0 to 6.5 ± 0.8 mmol·l\(^{-1}\), p < 0.01 in the whole group, but there were no further significant changes in lipid profiles in each group during the 6-month study period. Plasma creatinine concentrations were unchanged in the placebo group from baseline 102 ± 17 to 107 ± 24 µmol·l\(^{-1}\) at 6 months, but increased in the bezafibrate group from 108 ± 27 to 128 ± 36 µmol·l\(^{-1}\), p < 0.05. Plasma urea showed a similar trend from 7.1 ± 2.6 to 7.4 ± 2.4 mmol·l\(^{-1}\) at 6 months in the placebo group and from 8.1 ± 3.3 to 10.5 ± 4.3 mmol·l\(^{-1}\), p < 0.05, in the bezafibrate group. Urinary albumin: creatinine ratios (ACR), determined as the geometric mean of three consecutive early morning samples (results log-transformed), increased from 13.2 at baseline to 20.9 at 6 months in the placebo group, and decreased slightly from 24.0 to 20.9 in the bezafibrate-treated group. When the change in ACR during the study was compared between groups, the difference reached significance, p < 0.05.

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The mechanism of the small rise in plasma creatinine would not appear to be due to a tubular secretory defect for creatinine as plasma urea concentrations increased along with creatinine. Does this mean that bezafibrate affects renal function adversely in these subjects? If the renal lesion worsened, we would expect urinary albumin excretion to rise, which is the natural history of diabetic nephropathy [5] seen in the placebo group. However urinary albumin excretion on bezafibrate treatment was unchanged or fell slightly suggesting that bezafibrate is not necessarily harmful to the kidneys. The reason for the paradoxical changes in plasma creatinine and urinary albumin excretion on bezafibrate are not explained but we believe it should be used with caution in the presence of diabetic renal disease until the effects on renal function have been further elaborated.

References