



Fig. 1. Serum creatinine and treatment used in patient with Dent disease.

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Comment on: 'Lanthanum carbonate possibly responsible for acute liver failure in a patient with Child–Pugh stage A liver cirrhosis'

Sir,
De Leeuw and colleagues reported decompensation of existing liver disease in a patient with a complex history including alcohol-induced liver cirrhosis, pancreatitis and secondary diabetes [1]. The patient required hospitalization due to decreased consciousness and somnolence. The authors, noting a temporal association with lanthanum carbonate therapy, proposed that there was a causal relationship.

This patient report is highly confounded by a number of factors, including concomitant medication and hypophosphataemia, which are also credible explanations for the patient's presentation.

Firstly, the patient was taking lorazepam, which can cause coma in patients with reduced hepatic metabolism. Sec-

ondly, following dialysis the patient was profoundly hypophosphataemic. This is a recognized cause of irritability, paraesthesia, confusion, convulsions and coma [2].

Evaluation of the published data on lanthanum carbonate (FOSRENOL[®], Shire Pharmaceuticals, Basingstoke, UK) shows that the bioavailability is ~0.001% and the small fraction of lanthanum absorbed is not metabolized. Animal studies have demonstrated that the presence of lanthanum in the liver is consistent with hepatic excretion via a lysosomal transcellular transport mechanism [3,4].

A long-term follow-up of clinical trial cohorts has included liver function tests and has not demonstrated any evidence of acute or chronic liver toxicity during 2 years of therapy compared to standard therapy. In uncontrolled studies, subjects have been exposed to lanthanum carbonate for up to 6 years [5,6]. In addition to over 5000 subjects in clinical studies, there is now over 60000 patient-years of post-marketing experience with lanthanum carbonate.

Although no specific studies were done in patients with liver impairment, there is insufficient evidence to assume that lanthanum carbonate may contribute to a worsening of liver function in this patient population.

Conflict of interest statement. M.S., B.G. and R.D.P. are employees of Shire Pharmaceuticals.

Editorial Note: Dr De Leeuw *et al.* had been invited to reply to this letter but we did not receive a response in time.

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