there is a basis for a large trial in a population proposed by the correspondents. Our paper was also published to give hints on how to plan it and on its potential (large) sample size.

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Treatment of chronic hepatitis C in haemodialysis patients requires more ribavirin

Sir,
In a recent issue, Van Leusen et al. described a series of seven haemodialysis patients with chronic hepatitis C (HCV) who were treated with peginterferon alfa-2a (Pegasys®) and ribavirin (Copegus®), which resulted in sustained virological response (SVR) in five patients (71.5%) [1]. Despite their encouraging results, we think that higher ribavirin dosages would further boost SVR.

The authors report that their patient 1 did not respond to combination treatment of 135 µg peginterferon alfa-2a once a week and ribavirin 100–300 mg/day. We offered retreatment to this 39-year-old male. He was infected with HCV genotype 1b and had a low viral load (100 000 IU/ml). We started him on peginterferon alfa-2b (Pegintron®) 150 µg and ribavirin (Rebetol®) 400 mg/day. Within 2 weeks his plasma ribavirin levels reached 17.1 µg/ml. We therefore reduced ribavirin to 200 mg/day alternating with 400 mg/day. After 6 weeks ribavirin levels were 6.5 µg/ml, and dosage was maintained. Darbepoetin alfa dosage was increased from 20 µg to 150 µg/week. Haemoglobin decreased to 6.4 mmol/l at Week 12 and reached a nadir of 4.9 mmol/l after 28 weeks, but did not decrease further. Treatment was well tolerated and dose reduction or discontinuation due to adverse events was not needed. HCV RNA levels were undetectable after 8 weeks and he reached SVR. He received a renal transplant 1 year later.

HCV treatment in haemodialysis patients is crucial as these patients have a higher risk of developing cirrhosis and hepatocellular carcinoma. Timing of treatment is critical and needs to be performed prior to kidney transplantation as interferon can promote graft dysfunction [2]. Therefore, combination therapy should be considered in all HCV-infected ESRD patients.

Ribavirin is an essential component of HCV combination treatment and increases the SVR rates from 37% to 60% compared to interferon monotherapy [3]. Toxicity, especially haemolytic anaemia, adds a layer of complexity. This led some authors to suggest that ribavirin is contraindicated in ESRD patients because of the risk of ‘life-threatening’ haemolysis [2]. Our data and those of Van Leusen et al. suggest that ribavirin does not lead to uncontrollable haemolysis [1]. This corroborates with a recent study on 35 haemodialyzed HCV patients who were treated with peginterferon alpha-2a (135 µg weekly) and ribavirin 200 mg/day. A total of 26 patients developed severe anaemia and one patient uncontrolled anaemia (Hb 3.27 mmol/l) that led to treatment discontinuation, while the others required an increase of erythropoietin-alfa. This regimen was successful in 15 patients, while ribavirin was reduced to 200 mg every 2 days in 11 patients. SVR was reached in 97% [4].

From these data it appears that higher ribavirin plasma concentration increases the chance of viral clearance. In the study of Van Leusen et al., ribavirin was kept at a relatively low level (1.5–2.5 µg/ml) [1] while in our (successfully treated) case we reached at considerably higher levels, as in the 11 patients that necessitated ribavirin dose reductions plasma concentrations were 5.7 ± 1.5 µg/ml [4].

These considerations led to a Dutch nation-wide randomized controlled clinical trial that aims to compare the current standard therapy with a regimen that includes double dosage of ribavirin in naïve HCV genotype one and four patients [5].

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Reply

Sir,
We appreciate the interest shown in our publication by Slavenburg and Drenth and we share their opinion that a higher ribavirin (RBV) dose in combination with pegylated interferon (IFN) will lead to a better sustained response in the treatment of chronic hepatitis C in haemodialysis...