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CORRESPONDENCE

Increased Plasma Concentration of Ribavirin as a Result of Renal Dysfunction in Hepatitis C Virus Patients Treated With Telaprevir

To the Editor:

Pronounced anemia is observed in hepatitis C virus (HCV) patients treated with a triple therapy containing ribavirin (RBV), pegylated interferon (Peg-IFN), and telaprevir (TLV), when compared to patients treated with the dual therapy (RBV and Peg-IFN).[1] Mauss et al.[2] recently suggested, in HEPATOLOGY, that this could be a result of accumulation of RBV consequent to impaired renal drug elimination.

To confirm this hypothesis, the estimated glomerular filtration rate (eGFR),[3] hemoglobin (Hb), and RBV plasma concentration in 23 HCV genotype 1–infected patients treated with fixed doses of the triple therapy for 12 weeks and, successively, with the dual therapy until 48 weeks, were evaluated at weeks 4, 8, 12, 24, and 48.

eGFR decreased during the period of triple therapy from 100.8 ± 23.6 mL/min pretherapy to 88.5 ± 16.9, 75.7 ± 19.7, 83.4 ± 20.7 mL/min at weeks 4, 8, and 12, respectively ($P < 0.001$). When TLV was discontinued, eGFR returned to pretherapy levels (99.8 ± 24.6 and 104.9 ± 20.2 mL/min at weeks 24 and 48, respectively). Hb levels positively correlated with eGFR ($r = 0.191$; $P = 0.02$), showing a similar trend.

In contrast, RBV plasma concentrations increased when TLV was administered at 8 and 12 weeks ($2{,}777 \pm 1{,}093$ and $3{,}175 \pm 737$ ng/mL, respectively) and decreased ($P < 0.01$) at 24 and 48 weeks ($2{,}255 \pm 587$ and $1{,}872 \pm 622$ ng/mL, respectively) when TLV was suspended (see Fig. 1).

Moreover, significant inverse correlations were found between eGFR and Hb versus RBV ($P = 0.02$ and $P < 0.0001$ respectively).

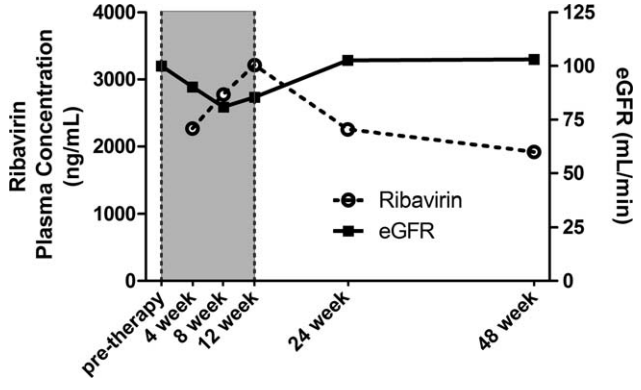

Fig. 1. RBV plasma concentration and eGFR during triple therapy containing TLV (gray window) and subsequent dual therapy.

These results are in agreement with those presented by Karino et al.,[4] who studied 68 patients during 8 weeks in triple therapy. Our study, which expanded therapy to 48 weeks using both the triple and dual regimens in sequence, concludes that plasma concentration of RBV and Hb levels are influenced by the decrease in renal function induced by TLV.

We can thus confirm the hypothesis of Mauss et al. and suggest use of eGFR, therapeutic drug monitoring, and dose adjustment of RBV to prevent onset of anemia induced by the triple therapy containing TLV.

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