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Response-guided therapy for acute hepatitis C: applying concepts from chronic treatment

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To the Editor

Each year, 17 000 individuals in the United States are infected with the hepatitis C virus (HCV), with the majority developing chronic infection (1). Current guidelines recommend treatment of acute HCV with interferon-based therapy, with a suggested duration of 12–24 weeks (2). This approach has proven effective in producing a sustained virological response (SVR) (3). Important predictors of SVR include a rapid virological response (RVR; absent HCV RNA at treatment week 4) and/or early virological response (EVR; absent RNA at week 12). While between 85 and 100% of patients will meet these thresholds (4, 5), it is unclear how to optimally treat patients who fail to demonstrate favourable viral kinetics. We applied response-guided therapy, adapted from studies in chronic HCV infection, to successfully treat a patient with acute HCV and a slow virological response to therapy.

A 49-year-old man was referred to the University of North Carolina for evaluation of acute HCV, identified during an attempted blood donation. The source of infection was initially unknown, although later traced to a routine nuclear cardiac stress test. Laboratory studies at initial referral included a negative anti-HCV antibody, an HCV RNA level of 5 million IU, alanine aminotransferase of 332 U/l, aspartate aminotransferase of 224 U/l and total bilirubin of 0.4 mg/dl. HCV genotype was 1a. Physical examination was normal except for a body mass index (BMI) of 37 kg/m². The patient was monitored for spontaneous clearance, which did not occur by 12 weeks post-exposure. His HCV antibody became positive during this interval, supporting the acuity of infection. Treatment was initiated with peginterferon α -2a (180 mcg weekly) and ribavirin (1400 mg daily), per our institutional protocol. Results of his viral kinetics are shown (Fig. 1). Notably, he failed to achieve an RVR or a complete EVR, although he did have a > 2 log reduction in HCV RNA at week 12 (partial EVR). At week 17, his RNA became undetectable. Treatment was continued for a total of 72 weeks. At 6 months post-treatment, his RNA remained undetectable, defining an SVR. This has persisted at 12-month post-treatment follow-up.

In managing this patient, we utilized data derived from the treatment of chronically infected HCV patients, where viral kinetics strongly correlate with treatment response. Patients who demonstrate an RVR will achieve an SVR between 85 and 95% of the time, for genotype 1 and non-genotype 1 infection respectively. Furthermore, lack of an EVR is the single greatest predictor of treatment failure in chronic HCV (6). This has led to the investigation of extended treatment for patients with a partial EVR. In this setting, extending treatment duration to 72 weeks has been shown to improve the likelihood of SVR. A similar approach may benefit patients who fail to achieve an RVR (7). Unfortunately, such individualized treatment strategies have not been fully evaluated in acute HCV infection.

Our patient had several predictors of poor treatment outcome, including high BMI, genotype 1 infection, high initial viral load and unfavourable viral kinetics. It is possible that a shorter duration of treatment (36–48 weeks) could have accomplished a similar outcome. However, in light of the high potential benefit of preventing chronic infection, we opted to prolong therapy for a duration utilized with slow virological responders in the chronic setting. The role of ribavirin for the treatment of acute hepatitis C is also unclear but has been utilized in this setting previously (8). Recognizing the importance of treating acute hepatitis C infection, further studies are needed to assess whether response-guided therapy may increase rates of SVR in the occasional slow virological responder.

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Fig. 1. Hepatitis C virus (HCV) RNA response to therapy (viral kinetics). Solid line, HCV RNA level by treatment week; dashed vertical lines, treatment weeks 4 and 12; dashed horizontal line, 2 log reduction in HCV RNA; △, exposure; ○, initial evaluation; □, treatment initiation.