

Taribavirin offers a safe, effective alternative for chronic hepatitis C

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Researchers at Cedars-Sinai Medical Center and 50 other centers found that weight-based dosing of taribavirin reduces rates of anemia while increasing sustained virologic response (SVR) in patients with chronic hepatitis C (HCV). Full details of this study are available in the October issue of *Hepatology*.

Chronic HCV is typically treated with ribavirin (RBV). When used in combination with peginterferon alfa (peg-IFN), RBV significantly enhances on-treatment virologic response and reduces relapse. However, RBV, particularly the combination of interferon and RBV, is associated with hemolytic [anemia](#), a significant toxicity resulting from the accumulation of RBV in red blood cells. Taribavirin (TBV), formerly known as viramidine, is a nucleoside analog and oral pro-drug of RBV that is less able to enter [red blood cells](#), and should therefore be associated with significantly less anemia.

This theory was demonstrated in two previous phase 3 trials. While statistically less anemia was observed in patients treated with TBV compared to RBV, the primary efficacy endpoint of these studies, a non-inferior SVR between the TBV and RBV, was not achieved. Detailed subgroup analyses of the data suggest fixed dosing as opposed to weight-based dosing, and the selection of an inadequate dose, are to blame. The present multi-center study explored several higher weight-based doses of TBV to determine a dosage regimen that was able to deliver comparable responses to RBV with fewer incidences of anemia.

A phase 2b randomized, open-label, active-controlled, parallel-group study was conducted in 278 treatment-naïve, genotype 1 patients stratified by body weight and baseline viral load at 51 centers in the United States between March 2007 and October 2008. Patients were randomized 1:1:1:1 to receive TBV (20, 25, or 30 mg/kg/day) or RBV (800 -1400 mg/day) with pegylated interferon alfa-2b for 48 weeks.

The primary efficacy endpoint was early virologic response (EVR) defined as the proportion of patients with at least a 2-log decrease from baseline in serum HCV RNA levels at treatment week 12. Additional efficacy endpoints included SVR, undetectable HCV RNA at treatment weeks 4, 24 and 48, and viral relapse for those who were responders at the end of treatment. A total of 86 (41%) of TBV patients and 25 (36%) of the RBV group completed treatment and follow up. The most commonly cited reasons for premature withdrawal were lack of response (29%) and adverse events (20%).

The present study demonstrated that weight-based dosing of TBV achieved comparable efficacy to RBV as demonstrated by SVR. This was observed in all three TBV weight-based dose treatment groups, which met the study's primary end-point. Patients treated with TBV had less than half the anemia compared to RBV treated patients. These results suggest weight-based dosing of TBV can significantly improve the tolerability of HCV treatment while maintaining efficacy. Specifically, the 25 mg/kg dose offered the optimal balance of efficacy and safety in this patient population.

Notably, fewer patients treated with TBV required dose reductions (13-28%) compared to 32% of patients treated with RBV. Less frequent dose modification in patients treated with TBV may alleviate the need to utilize erythropoiesis-stimulating agents (ESAs). Several studies have demonstrated the use of ESAs can significantly decrease the need to dose reduce RBV and leads to an improvement in the quality of life

during HCV treatment, but fails to improve the SVR. The use of ESAs also adds significant cost to HCV treatment and is associated with serious adverse events including thrombosis and red cell aplasia.

Lead investigator Dr. Fred Poordad concludes, "These data suggest TBV may be an effective agent to substitute for RBV in the future and could be incorporated in upcoming trials utilizing emerging small molecules for HCV treatment."

Editorial author Dr. Paul Kwo comments, "If TBV can be shown to preserve or improve efficacy rates in combination with direct-acting antiviral agents (DAAs) and Peg IFN, with lower rates of anemia, the use of TBV in these clinical settings would be a welcome addition to the HCV armamentarium as we begin to expand the HCV populations that we treat. TBV may have a role in populations particularly sensitive to ribavirin-related anemia. However, with the commencement of several trials comprising of multiple combinations of DAAs with and without pegIFN/RBV, and the development of newer protease inhibitors with potentially lower rates of anemia, the role of TBV remains less precisely defined and could potentially have a finite life cycle."

More information: Article: "Virologic Response Rates of Weight-Based Taribavirin versus Ribavirin in Nad've Chronic Hepatitis C Genotype 1 Patients." Fred Poordad, Eric Lawitz, Mitchell Shiffman, Tarek Hassanein, Andrew Muir, Bruce Bacon, Jaime Heise, Deanine Halliman, Eric Chun, Janet Hammond. *Hepatology*; Published Online: June 30, 2010 ([DOI: 10.1002/hep.23827](https://doi.org/10.1002/hep.23827)); Print Issue Date: October 2010. [onlinelibrary.wiley.com/doi/10 ... 2/hep.23827/abstract](https://onlinelibrary.wiley.com/doi/10.1002/hep.23827/abstract)

Editorial: "The Next Step for Taribavirin." Paul Kwo and Rakesh Vinayek. *Hepatology*; Published Online: September 7, 2010 ([DOI: 10.1002/hep.23957](https://doi.org/10.1002/hep.23957)); Print Issue Date: October 2010. [onlinelibrary.wiley.com/doi/10 ... 2/hep.23957/abstract](https://onlinelibrary.wiley.com/doi/10.1002/hep.23957/abstract)

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