Anemia Top Side Effect of HCV Antivirals

By John Gever, Deputy Managing Editor, MedPage Today
Published: April 26, 2013

AMSTERDAM -- Two years after direct-acting antiviral drugs for hepatitis C virus (HCV) infection hit the U.S. market, anemia has been far and away their most significant adverse effect, researchers said here.

Outcomes in more than 1,400 U.S. patients taking a HCV protease inhibitor in routine practice for chronic infection indicated that more than half had experienced anemia, whether they received boceprevir (Victrelis) or telaprevir (Incivek), according to Michael W. Fried, MD, of the University of North Carolina in Chapel Hill.

Triple therapy with one of these drugs plus ribavirin and pegylated interferon is now the standard of care for HCV genotype 1.

Although severe skin rashes have been telaprevir's most talked-about side effect, prompting the FDA to add a boxed warning to the drug's label, severe anemia was much more common. Of the 1,082 patients in the study taking telaprevir, 27 showed severe anemia, compared with five patients developing severe rash, Fried and colleagues found.

Among 344 patients on boceprevir, six developed severe anemia.

These data were collected by a consortium of 44 academic centers and 59 community-based clinics in the U.S., which have sought to enroll all patients receiving these drugs. The only exclusion criteria were consent refusal or participation in another study of HCV therapies.

Beyond that, clinicians were free to prescribe dosing regimens and manage adverse effects according to their own judgment.

Anemia in most patients was treated mainly by reducing ribavirin dosages, for patients with cirrhosis as well as those without (65% and 54%, respectively).

Clinicians resorted to erythropoietin-type drugs in 13% of cirrhotic patients and 19% of those with no cirrhosis. Transfusions were given to 17% and 8% of cirrhotic and noncirrhotic patients, respectively.

Baseline cirrhosis was a significant risk factor for severe anemia and premature discontinuation of treatment. Fried and colleagues found odds ratios of 1.5 to 2.2 (all $P<0.05$) for risk of these outcomes as well as for any serious adverse event and for early discontinuation attributed to adverse effects.

Some 11% of the 550 patients with cirrhosis developed decompensation on treatment, compared with 1% of noncirrhotic patients.

Fried and colleagues also found virologic response rates in their patients to be similar to, if not better than, those seen during the drugs' clinical trials.

Patients taking telaprevir had HCV viral loads below the limits of detection or quantitation at rates of 91% to 96% at treatment week 12, depending on prior treatment history.

Corresponding data for boceprevir patients ranged from 63% to 87%.

About one-quarter of patients in the study stopped all therapy prematurely. Lack of efficacy and adverse events accounted for 35% and 40% of discontinuations, respectively.

At a press briefing, Laurent Castera, MD, of Centre Hospitalier Universitaire de Bordeaux in France, who was not involved with the study, said it was noteworthy in representing a real-world patient population, as opposed to the carefully selected samples enrolled in clinical trials.

Despite the broader mix of patients seen in the post-marketing study, Castera said the efficacy results were "comparable" to those seen in the two drugs' registration trials. Rates of anemia and other adverse events also tracked closely with previous trial results, in which some degree of anemia occurred with both drugs in half of patients.