New Hep C Treatment Guidelines Spell Out Incivek and Victrelis Use

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Revised treatment guidelines from the American Association for the Study of Liver Diseases (AASLD) outline a significant change in the standard of care for people with genotype 1 chronic hepatitis C virus (HCV) infection. Instead of 48 weeks of pegylated interferon and ribavirin, treatment should also include one of the two new protease inhibitors (PIs)—either Incivek (telaprevir) or Victrelis (boceprevir)—with the length of therapy based on the results of viral load testing at different time points, depending on which PI is used.

Generally, people can discontinue therapy after 24 weeks, provided that their HCV viral load is undetectable after four weeks of therapy with a PI-inclusive regimen and that the virus remains undetectable for the remaining 20 weeks. Forty-eight weeks of treatment is still recommended for people who have cirrhosis, and for certain repeat treatment-takers (called null responders).

The updated AASLD guidelines, published in October in *Hepatology*, were issued for health care providers treating people with either Incivek or Victrelis, both of which were approved in May 2011 for use in combination with pegylated interferon and ribavirin. Incivek and Victrelis have dramatically increased cure rates for both first-time and repeat treatment-takers with chronic HCV genotype 1 infection. However, adding a third drug also makes HCV treatment more complicated for patients and their doctors.

Because of these complications, which include side effects and the development of HCV drug resistance to the protease inhibitors, AASLD recommends curtailing HCV treatment when it is very unlikely to work. Since these “stopping rules” differ for each drug, clear guidance is provided for when to stop therapy with both drugs.

The updated AASLD guidelines refer clinicians to the drugs’ labeling, or detailed package insert, for information on managing side effects, although the guidelines authors do provide their own guidance on managing anemia. Anemia is a common side effect from ribavirin and the HCV protease inhibitors. During hepatitis C treatment, if anemia develops, people are either treated with a red blood cell growth factor, such as Procrit (erythropoietin), or given a lower dose of ribavirin. The authors noted that cure rates were similar no matter which strategy was used to manage anemia. Since growth factors are costly and add side effects, AASLD recommends

reducing the ribavirin dose to manage anemia while maintaining full-dose Incivek or Victrelis.

The guidelines also stress that clinicians and their patients can use IL-28B genotype testing—a blood test that can predict responses to HCV treatment with pegylated interferon, ribavirin and either Incivek or Victrelis—to gain more information on the likelihood of treatment effectiveness and the length of treatment. The authors caution, however, that IL-28B testing should not be used to withhold PIs from patients who have more favorable IL-28B results (for example, a "CC" genotype) and may be more likely to be cured with pegylated interferon and ribavirin alone, given that adding a PI significantly boosts cure rates in people with all IL-28B variations, including the harder-to-treat "CT" and "TT" genoytpes.

In the United States, an estimated 70 percent of people with hepatitis C have genotype 1. Before Incivek and Victrelis were approved, genotype 1 was difficult to treat; cure rates were less than 50 percent. Now, adding a protease inhibitor to pegylated interferon and ribavirin means that first-time treatment-takers are much more likely to be cured and they may be able to shorten treatment from 12 to six months. Hepatitis C protease inhibitors will also help people who were unsuccessfully treated in the past.

Marc G. Ghany, from the Liver Diseases Branch of the National Institute of Diabetes and Digestive and Kidney Diseases, coauthored the updated recommendations with four colleagues. Ghany and his peers note that the update is "intended to be flexible, in contrast to standards of care, which are inflexible policies to be followed in every case."

Ghany and his coauthors based their recommendations on their years of experience treating hepatitis C, and on published results from clinical trials. Their recommendations were based on the strength of available scientific evidence, as well as their potential risks and benefits. As such, these guidelines offer a thorough overview of the results from clinical trials, followed by specific recommendations for treating different groups of patients with each drug (since they are used differently).

Guidance on HCV treatment for special populations is limited because of a lack of data in people coinfected with HIV and hepatitis C, transplant recipients and people with decompensated cirrhosis, but the updated guidelines do address some key aspects of HCV treatment, such as how to determine the proper duration of treatment and the best time to stop it, as well as how to manage common side effects from the new drugs.

The guidelines also underscore the risk of combining Incivek or Victrelis with certain drugs that are commonly used by people with hepatitis C, and the guides provide additional resources for medical providers to help avoid drug interactions that can prevent drugs from working or increase their side effects.

Unfortunately, the updated guidelines do not offer guidance on adherence, although it is crucial for successful HCV treatment. Incivek and Victrelis must be taken every eight hours, along with weekly injections and twice-daily ribavirin, often by people who already use additional

medications.

Now that a cure is more likely for people with HCV genotype 1, the demand for treatment is sure to increase, and more non-specialist providers may be called upon to care for HCV patients. The revised guidelines are an important resource, since they incorporate the latest research results into clear and handy recommendations for busy clinicians.
