Revised U.S. Guidelines Make Key HIV and Hep C Treatment Recs

April 2, 2012 By Tim Horn

Important preliminary recommendations involving the use of hepatitis C protease inhibitors among people living with HIV are provided by U.S. Department of Health and Human Services panelists in the March 27 update to the Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. Though both Incivek (telaprevir) and Victrelis (boceprevir) are listed as options, the panelists draw upon drug-drug interaction data to conclude that Incivek should be used instead of Victrelis when ARV regimens that include Norvir (ritonavir)–boosted Reyataz (atazanavir) or efavirenz (found in Sustiva and Atripla) are being used to treat HIV.

Though the hepatitis C protease inhibitors aren't approved for people coinfected with HIV and the hepatitis C virus (HCV) and are still being explored in clinical trials for this population, results thus far have been encouraging. According to preliminary data from two randomized studies presented at the 19th Conference on Retroviruses and Opportunistic Infections last month in Seattle, the addition of either Incivek or Victrelis to mainstay therapies pegylated interferon and ribavirin improve sustained virologic response (SVR), or viral cure, rates by roughly 30 percent.

A central concern with these important additions to the hepatitis C treatment arsenal is their drug-drug interaction profiles. As these drugs are broken down, or metabolized, via the same pathways as many HIV medications, the likelihood of interactions—resulting in reduced treatment efficacy and a higher risk of side effects—is significant.

Earlier this year, a team of experts issued preliminary guidelines regarding the use of hepatitis C protease inhibitors in concert with HIV regimens. These recommendations, however, were subsequently withdrawn by the authors and pulled from the online version of Clinical Infectious Diseases, after data emerged indicating that Victrelis's interactions with HIV medications were more pronounced than was originally anticipated.

Based on currently available data, the DHHS panelists provide new, preliminary guidelines for people living with HIV requiring a protease inhibitor–inclusive combination therapy to treat genotype 1 HCV infection.

People living with HIV not currently using ARV therapy may use either Victrelis or Incivek, the panelists note.

People with HIV who are taking two nucleoside reverse transcriptase inhibitors (NRTIs) plus Isentress (raltegravir) can also use either Victrelis or Incivek. That's because Isentress, which is Merck's approved integrase inhibitor, has a unique metabolism pathway in the body and has been shown in studies not to have significant interactions with either Victrelis or Incivek.

If Norvir-boosted Reyataz is used, only Incivek should be prescribed in combination with pegylated interferon and ribavirin to treat HCV. Victrelis, because of recently reported interactions with all Norvir-boosted HIV protease inhibitor regimens (including Reyataz), should be avoided.

The panelists add that, when combined with Norvir-boosted Reyataz plus two NRTIs, the standard dose of Incivek should be used: 750 milligrams (mg) three times a day.

If efavirenz—either as Atripla or Sustiva plus two NRTIs—is being used, Incivek is the only hepatitis C protease inhibitor that should be prescribed. However, because of a moderate drug-drug interaction between the two, the Incivek dose should be increased to 1,125 mg three times daily.

Other Considerations and Recommendations

Though not officially evidence-based recommendations—guidance based on sound, scientific conclusions—the expert panelists offer up a handful of key considerations people living with HIV/HCV coinfection and their health care providers may wish to consider when making treatment decisions:

- If HCV disease is minimal—no or minimal liver fibrosis, confirmed by liver biopsy—the panelists suggest considering deferral of HCV treatment "given rapidly evolving HCV drug development."

- If good prognostic factors for HCV treatment response are present—for example, a test confirming the IL-28B CC (as opposed to the CT to TT) genotype and a low (below 400,000) HCV viral load—the panelists suggest considering the use of pegylated interferon plus ribavirin alone for those with genotype 1 HCV infection.

- Because of differences between Incivek and Victrelis—for example, the side effect profiles of the drugs are not the same—having both available as options may be important to coinfected individuals requiring HCV treatment. "On the basis of [ARV treatment] history and HIV genotype testing results, if possible, consider switching to the [ARV] regimens listed [in the guidelines] to permit the use of boceprevir or telaprevir."

- Among coinfected individuals with complex ARV treatment histories or resistance to multiple

HIV drugs, “consultation with experts regarding the optimal strategy to minimize the risk of HIV breakthrough may be needed,” the panelists write. “In such patients, telaprevir may be the preferred [HCV protease inhibitor] because its duration of use (12 weeks) is shorter than that of boceprevir (24 to 44 weeks).”

The revised guidelines also reiterate the importance of ARV therapy among people coinfected with both viruses, independent of HCV treatment decisions. “[ARV therapy] may slow the progression of liver disease by preserving or restoring immune function and reducing HIV-related immune activation and inflammation,” the panelists write. “For most HIV/HCV-coinfected patients, including those with cirrhosis, the benefits of [ARV therapy] outweigh concerns regarding drug-induced liver injury (DILI). Therefore, [ARV therapy] should be considered for HIV/HCV-coinfected patients, regardless of CD4 count.”

The panelists note, however, that “combined treatment of HIV and HCV can be complicated by large pill burden, drug interactions and overlapping toxicities.” In turn, though HCV treatment is recommended regardless of a coinfected patient’s CD4 cell counts, for those not yet on HIV treatment with CD4 cell counts greater than 500, “some clinicians may choose to defer [ARV therapy] until completion of HCV treatment.”

Conversely, the panelists add, “[i]n patients with lower CD4 counts”—such as those with fewer than 200 CD4s—“it may be preferable to initiate [ARV therapy] and delay HCV therapy until CD4 counts increase as a result of [HIV treatment]."
