HIV/HCV Coinfection – Viral Interactions and Therapy

As HIV-infected patients live longer and healthier lives with combination antiretroviral therapy, non-HIV-related illnesses, chief among them liver disease caused by chronic hepatitis C, contribute to significant comorbidity and increased mortality. For the last 15 years, liver disease has been rising as a cause of death among HIV-infected individuals.(1) The incidence of liver failure and HCC in this population has increased significantly in recent years.(2)

Hepatitis C virus (HCV) coinfection rates among HIV-infected patients depends on the mode of transmission of HIV and ranges from 7% for sexual transmission to 91% for injection drug use.(3) HIV coinfection complicates HCV-related liver disease in that disease progression tends to be more rapid. Fibrosis progression is accelerated(4) as is progression from cirrhosis to liver failure, and once liver decompensation has set in; survival is shorter in HIV/HCV-coinfected patients compared to patients with HCV monoinfection.(5)

Chronic hepatitis C can be cured with antiviral therapy, and this goal has particular importance for HIV/HCV-coinfected patients who are at greater risk of severe complications. In the era of peginterferon and ribavirin (PEG/RBV), rates of sustained viral response (SVR) have been lower than for HCV-monoinfected patients, about 30% in HCV genotype 1 and 67% in genotypes 2 and 3.(6) As a result, enthusiasm for treating HIV/HCV patients for hepatitis C has been limited.

Since May-2011, the two HCV protease inhibitors boceprevir (BOC) and telaprevir (TPV) have been available for combination therapy with PEG/RBV, which is now considered standard of care for patients infected with HCV genotype 1. Both drugs are metabolized through the CYP 3A4 enzyme system, and as a result they have drug-drug-interactions (DDIs) with multiple other medications. These interactions make dose adjustments necessary for certain drugs and disallow others altogether. These DDIs also exist with many antiretroviral drugs, limiting the antiretroviral regimens an HIV/HCV-coinfected patient can be on when being treated with triple HCV therapy including boceprevir or telaprevir. For example, the commonly prescribed HIV non-nucleoside reverse transcriptase inhibitor efavirenz induces CYP 3A4 and lowers levels of telaprevir, requiring a dose adjustment from 750 mg every 8 hours to 1125 mg every 8 hours in the presence of efavirenz. The HIV protease inhibitors darunavir and fosamprenavir are contraindicated in combination therapy with telaprevir, since they significantly lower telaprevir levels, and their levels are lowered as well in the presence of telaprevir.(7) Similar DDIs between have been described between efavirenz and certain HIV protease inhibitors and boceprevir.

Both HCV protease inhibitors have been tested in combination with PEG/RBV in HIV/HCV-coinfected patients in two small phase 2 trials. The two studies showed similar SVR rates in triple therapy (BOC/PEG/RBV, 61%; TPV/PEG/RBV, 74%) as had been reported in the phase 3 trials in HCV-monoinfected patients (BOC, 66%; TPV; 75%). In each study, there was about a 30 percent point increase in SVR rate in triple therapy compared to PEG/RBV dual therapy,
similar to the phase 3 trials in HCV monoinfection. Safety data in HIV/HCV patients were also similar to the experience in HCV patients with anemia, rash, and taste disturbance being more common in the triple therapy group. In addition, in HIV/HCV patients, there was an increase in influenza-like symptoms in the triple therapy group.(8, 9)

Currently, phase 3 trials are underway in HIV/HCV genotype 1 patients that test the combination of PEG/RBV with the HCV protease inhibitors telaprevir, simeprevir, and faldaprevir as well as the HCV NS5a inhibitor daclatasvir. Furthermore, phase 2 pilot studies are ongoing that treat HIV/HCV patients with interferon-free combinations of direct antiviral agents (DAAs) and ribavirin.

Acute hepatitis C of HIV-infected individuals following sexual exposure to HCV-infected partners has been described in several epidemics of men who have sex with men. Treatment with peginterferon with or without RBV leads to SVR rates of 65% in genotypes 1 & 4 and of 81% in genotypes 2 & 3.(10)

References