

HCV/HIV Co-infection: Risks and Treatment Options

OVERVIEW

Liver disease is the leading cause of non-AIDS related death among persons infected with human immunodeficiency virus (HIV).¹ An important cause of liver-related mortality in this population is hepatitis C virus (HCV) co-infection, which affects an estimated 4-5 million people worldwide, including more than 250,000 persons in the United States.^{2,3} Patients with HCV/HIV co-infection have a 35% higher risk of mortality compared to persons with HIV mono-infection,⁴ and among persons with HCV infection who have an AIDS diagnosis, the relative risk of mortality increases to 50%.⁵

Hepatitis and hepatic fibrosis progress more rapidly among patients with HCV/HIV co-infection compared with patients who have HIV mono-infection, which increases the risk of cirrhosis, end-stage liver disease, hepatocellular carcinoma, and liver-related death in the absence of transplantation.^{6,7} Although sustained virologic response (SVR) is the goal of HCV treatment, patients with HCV/HIV co-infection often have low rates of SVR when treated with the standard HCV therapy of pegylated interferon plus ribavirin (pegIFN/ribavirin).⁸⁻¹² However, there has been a rapid emergence of new therapies for both HCV mono-infection and HCV/HIV co-infection.¹³ A number of clinical trials of direct-acting antiviral agents for HCV and HCV/HIV are underway or have recently reported clinically significant results.¹⁴⁻¹⁹

The epidemiology of HCV also is evolving. Although injection drug use remains the primary mode of transmission, sexual transmission – once considered rare for HCV – has increased, particularly among certain subgroups of HIV-positive men who have sex with men (MSM).¹⁹⁻²² A recent retrospective study reported a 1.6% annual incidence of HCV/HIV co-infection among MSM, the highest rate ever reported by studies of MSM in the United States.²³ Molecular studies indicate that HCV/HIV co-infected patients have higher rates of T-cell activation and exhaustion compared with persons who are healthy or mono-infected with either virus, and this difference may account for increased levels of HCV viremia seen in persons with HIV infection.^{24,25} It is thought that increased viremia, in turn, increases the likelihood of HCV transmission during high-risk sexual activities.^{19,25}

Clinicians must stay abreast of changes in the epidemiology and treatment of HCV/HIV co-infection to be able to best diagnose and treat this condition. However, studies indicate that substantial knowledge and practice gaps persist among clinicians who treat HCV and HCV/HIV co-infection. This continuing medical education program will educate physicians, pharmacists, nurses, and other health care professionals about the prevalence, pathology, risk factors, current therapies, and new drug development efforts for patients co-infected with HCV and HIV.

RESEARCH REVIEW (EXCERPT)

From 1998 until recently, pegIFN/ribavirin was the standard treatment for HCV infection.²⁶ However, therapeutic outcomes have been suboptimal for many patients with HCV/HIV co-infection due to therapeutic contraindications, low rates of treatment initiation, and reported SVR rates of approximately 14-30%.^{9-13,27-29}

In the past several years, direct-acting antiviral agents have shown promise for the treatment of both HCV mono-infection and HCV/HIV co-infection.¹⁴ However, these protease inhibitors also are associated with adverse events and drug interactions in co-infected patients, and more data are needed on their potential to achieve SVR in this population.

Multiple direct-acting antivirals are being investigated for HIV/HCV co-infection. Notable findings from these studies and ongoing late-stage trials of interest are summarized here.

Boceprevir

- Boceprevir targets the nonstructural NS3 protease of HCV, which plays major role in virus replication.³⁰
- In May 2011, boceprevir was the first protease inhibitor approved by the FDA to be used in combination with pegIFN/ribavirin for the treatment of chronic HCV genotype 1 infection.³¹
- In April 2012, the FDA recommended against co-therapy with boceprevir and certain ritonavir-boosted HIV protease inhibitors due to the risk of decreased efficacy secondary to CYP3A4/5 inhibition.³²
- In a phase IIa study, 98 patients with HIV/HCV were randomly assigned to 4 weeks of pegIFN/ribavirin followed by 44 weeks of combination therapy of 800 mg boceprevir every 8 hours (n = 64) or placebo (n = 34) plus pegIFN/ribavirin.^{14,33} The results showed that 12 weeks after ending boceprevir plus pegIFN/ribavirin therapy, 61% of patients with HIV/HCV co-infection had SVR (defined as undetectable HCV RNA), compared with 27% of patients receiving pegIFN/ribavirin only. Virologic breakthrough occurred in 9% of patients during treatment with boceprevir, and relapse occurred in 5% of patients after therapy ended.
- An interim analysis was reported in March 2013 of a phase II trial to assess the efficacy and safety of efficacy and safety of boceprevir plus pegIFN/ribavirin in HCV/HIV co-infected patients who previously failed pegIFN/ribavirin therapy.¹⁸ Researchers reported that up to week 16, response rates and tolerability profiles were similar between the two therapies.
- Boceprevir is associated with higher rates of anemia and gastrointestinal symptoms in patients with HCV and HIV compared to HCV-monoinfected patients.³⁴

GAP ANALYSIS (EXCERPT)

Practice Gap	Type of Gap	Learning Objective	Desired Outcome
<p>Health providers must understand risk factors for progression of HCV disease in order to evaluate and select appropriate treatments.³⁵</p> <p>Providers lack current data on the pathology and progression of HCV/HIV co-infection and do not believe study findings apply to their own patients.³⁶</p>	Knowledge	Describe the pathology of HCV/HIV co-infection and its effects on progression of hepatic disease, severity, and mortality.	Clinicians understand the importance of early diagnosis of HIV/HCV co-infection and the need to educate patients about appropriate disease management.

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