

Antiretroviral Considerations in Patients with Coinfections

HEPATITIS B (HBV)/HIV COINFECTION (Updated December 1, 2007)

It is not clear that treatment of HBV improves the course of HIV infection, nor is there evidence that treatment of HIV alters the natural history of chronic HBV. However, several liver-associated complications that are ascribed to flares in HBV activity or to toxicity of antiretroviral agents can affect the treatment of HIV in patients with HBV coinfection. These include the following:

- Emtricitabine, lamivudine, and tenofovir have activity against both HIV and HBV. Discontinuation of these drugs may potentially cause serious hepatocellular damage resulting from reactivation of HBV [1-3];
- Lamivudine-resistant HBV is observed in approximately 40% of patients after 2 years of lamivudine monotherapy for chronic HBV and in approximately 90% after 4 years when it is used as the only active drug for HBV in coinfecting patients [4, 5];
- Entecavir has activity against HIV, and its use in patients with dual infection has been associated with selection of the M184V mutation that confers resistance to lamivudine and emtricitabine [6, 7]. Therefore, entecavir should be used only with a fully suppressive antiretroviral regimen in HIV/HBV-coinfecting patients.
- Immune reconstitution can be associated with elevation in transaminases, possibly because HBV is primarily an immune-mediated disease [8]; and
- Many antiretroviral drugs can cause increases in transaminase levels. The rate and magnitude of these increases are higher with HBV coinfection [9, 10]. The etiology and consequences of these changes in liver function tests are unclear, because continuation of therapy may be accompanied by resolution of the changes. Nevertheless, some experts suspend the implicated agent(s) when the ALT is increased to 5–10 times the upper limit of normal. However, in HIV/HBV-coinfecting persons, increases in transaminase levels can herald HBeAg seroconversion, so the cause of the elevations should be investigated prior to the decision to discontinue medications. HBeAg seroconversion can be evaluated by checking HBeAg and anti-HBe as well as HBV DNA levels.

Treatment Recommendations for HBV/HIV Coinfecting Patients

- All patients with HBV should be advised to abstain from alcohol; should receive hepatitis A vaccine if found not to be immune at baseline (i.e., absence of hepatitis A total or IgG antibody); should be advised on methods to prevent HBV transmission (which do not differ from those to prevent HIV transmission); and should be evaluated for the severity of HBV infection.
- **If neither HIV nor HBV infection requires treatment:** Monitor the progression of both infections. If treatment becomes necessary for either infection, follow the guidelines listed in the scenarios below.
- **If treatment is needed for HIV but not for HBV:** The combination of tenofovir and emtricitabine or tenofovir and lamivudine should be used as the NRTI backbone of an antiretroviral regimen, which will result in treatment of both infections. To avoid development of HBV-resistant mutants, none of these agents should be used as the only agent with anti-HBV activity in an antiretroviral regimen.
- **If treatment for HBV is needed:** Patients who need treatment for HBV infection should also be started on a fully suppressive antiretroviral regimen that contains NRTIs with activity against both viruses: for example, tenofovir plus either emtricitabine or lamivudine. The use of lamivudine, emtricitabine, or tenofovir as the only active anti-HBV agent should be avoided because of the risk for resistance. If tenofovir cannot be used, another agent with anti-HBV activity should be used in combination with lamivudine or emtricitabine for treatment of HBV infection. Management of HIV should be continued with a combination regimen to provide maximal suppression.
- **Treating only HBV:** In instances when HIV treatment is not an option or is not desirable, pegylated interferon-alpha may be used for the treatment of HBV infection, as it does not lead to the emergence of HIV or HBV resistance. Adefovir dipivoxil is active against HBV but not against HIV at the 10mg dose; however, there is a theoretical risk for development of HIV resistance, as it has anti-HIV activity at higher doses and is related to tenofovir. Because of

the risk for HIV drug resistance, the use of emtricitabine, lamivudine, tenofovir, or entecavir without a full combination antiretroviral regimen should be avoided.

- **Need to discontinue emtricitabine, lamivudine, or tenofovir:** Monitor clinical course with frequent liver function tests and consider the use of interferon, adefovir dipivoxil, or telbivudine to prevent flares, especially in patients with marginal hepatic reserve.

References

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HEPATITIS C (HCV)/HIV COINFECTION (Updated October 29, 2004)

Long-term studies of patients with chronic HCV infection show that approximately 33% of the patients progress to cirrhosis at a median time of less than 20 years [1]. This rate of progression increases with older age, alcoholism, male sex, and HIV infection [1-3]. A meta-analysis demonstrated that the rate of progression to cirrhosis with HCV/HIV coinfection was about threefold higher when compared with patients who are seronegative for HIV [2]. This accelerated rate is magnified in patients with low CD4 counts. Chronic HCV infection also complicates HIV treatment by the increased frequency of antiretroviral-associated hepatotoxicity [4]. Multiple studies show poor prognosis for HCV/HIV coinfection in the era of combination antiretroviral therapy. It is unclear if HCV adversely affects the rate of HIV progression [5, 6] or if this primarily reflects the impact of injection drug use, which is strongly linked to HCV infection [7, 8]. It is also unclear if antiretroviral therapy improves the attributable morbidity/mortality for untreated HCV.

Assessment of HCV/HIV Coinfection

Patients with HCV/HIV coinfection should be advised to avoid or limit alcohol consumption, use appropriate precautions to prevent transmission of both viruses to others, and should be given hepatitis A and B vaccine if found susceptible. All patients with HCV, including those with HIV coinfection, should be evaluated for HCV therapy.

Standard indications for HCV therapy in the absence of HIV infection are detectable plasma HCV RNA and a liver biopsy showing bridging or portal fibrosis. ALT levels may be elevated in association with HCV infection. However, ALT levels do not accurately reflect the severity of HCV-associated liver disease. Liver biopsy is important for HCV therapeutic decision making but is indicated only if the patient is considered a treatment candidate based on multiple other variables including severity and stability of HIV disease, other comorbidities, probability of adherence, and if there are contraindications to interferon-alpha, one of the drugs available for treatment of HCV.

Clinical trials in patients with HCV/HIV coinfection using pegylated interferon plus ribavirin for 48 weeks show sustained virologic response (SVR) rates of 60%–70% for HCV genotype 2/3 but only 15%–28% for genotype 1 [9, 10].