Considerations for Antiretroviral Use in Patients with Hepatitis B Virus & Human Immunodeficiency Syndrome Co-infection

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HBV & HIV

- Hepatitis B virus (HBV) is the leading cause of chronic liver disease worldwide.
- Persons with HIV infection are at increased risk for :
- Developing chronic HBV Infection
- Detectable HBeAg
- Lower rate of seroconversion to anti-Hbe
- Increased risk of HCC, liver- related mortality and morbidity

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HBV & HIV

- In HIV/HBV coinfection, monitoring and treatment are also focused on the simultaneous treatment of both viruses.

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Treating Disease

- Treating HBV Infection Indication for Therapy:
  - All HIV/HBV coinfected patients, regardless of CD4 count and HBV DNA level .

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Special Considerations with Regard to Starting ART

- Preferred Regimen:
- Because both tenofovir and emtricitabine have anti-HBV activity, the combination is also the treatment of choice for HIV/HBV coinfected patients regardless of CD4 and HBV DNA level .

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HBV & HIV

- Patients receiving ART should continue HBV therapy indefinitely because relapses after response occur, particularly in those with lower CD4 cell counts.

Additionally, discontinuation of nucleos(t)ide analogue therapy is associated with a HBV flare in approximately 30% of cases, with loss of the benefit accrued from previous anti-HBV treatment and possible decompensation of liver disease.

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Regimens that are Not Recommended

- Tenofovir (TDF and TAF), entecavir, lamivudine, emtricitabine, and telbivudine should not be used alone in the absence of a fully suppressive ART regimen because of the development of HIV-resistance mutations.
- Other HBV treatment regimens include adefovir in combination with lamivudine or emtricitabine or telbivudine in addition to a fully suppressive ART regimen; however, data on these regimens in persons with HIV/HBV coinfection are limited.
- Therefore, Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents (the Panel) does not recommend these drugs/regimens for HIV/HBV coinfected patients.

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HBV & HIV

- HBV reactivation can occur during treatment of HCV infection in the absence of HBV-active drugs; therefore, all HBV patients who will be treated for HCV should be on HBV-active ART at the time of HCV treatment initiation .

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HBV & HIV

- Alternative Therapy If the Patient Refuses ART:
- • Anti-HBV therapy is indicated for elevated ALT, and HBV DNA >2000 IU/mL, significant liver fibrosis, advanced liver disease, or cirrhosis .
- Peg-IFN-alfa 2a 180 mcg SQ once weekly for 48 weeks

Or

- Peg-IFN- alfa 2b 1.5 mcg/kg SQ once weekly for 48 weeks
- Directly acting HBV drugs (such as 3TC, FTC, TAF, TDV, entecavir, adefovir, and telbivudine) must not be given in the absence of a fully suppressive ART regimen to avoid selection of drug resistant HIV .

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Monitoring of Response to Therapy

- In order to prevent emergence of drug-resistant variants and evaluate response for patients on nucleos(t)ide analogues, treatment response should be monitored by testing for HBV DNA at 3 to 6 month intervals.

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Immune Reconstitution Inflammatory Syndrome (IRIS)

- Return of immune competence after ART (or after steroid withdrawal or chemotherapy) can lead to reactivation of HBV-associated liver disease. Any immune reconstitution can lead to a rise in serum aminotransferases, so called "hepatitis flare," which constitutes IRIS in HIV/HBV-coinfected persons.
- Distinguishing between ART-associated hepatotoxicity or other causes of hepatitis (acute hepatitis A, C, D, or E virus, EpsteinBarr virus, herpes simplex virus, cytomegalovirus) and IRIS may be difficult.
- The major problem in managing ALT flares is distinguishing between drug-induced liver injury and HBV reactivation, IRIS, emergence of HBV drug resistance, and HBeAg seroconversion.

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Preventing Exposure

- HBV is primarily transmitted through percutaneous or mucosal exposure to infectious blood or body fluids. Therefore, HIV-infected patients should be counseled about transmission risks for HBV and encouraged to avoid behaviors associated with such transmission. Such counseling should emphasize sexual transmission as well as the risks associated with sharing needles and syringes, tattooing, or body-piercing.
- All family members and sexual contacts of patients with HBV should be screened and all susceptible contacts should receive HBV vaccines regardless of whether they are HIV- infected.
- All HIV-infected patients susceptible to HBV should be receive hepatitis B vaccination.
- All HIV-infected patients should be screened for hepatitis B, and screening should include HBsAg, antiHBs, and anti-HBc.

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Preventing HBV Infection

- Indications for HBV Vaccination:
- Patients without chronic HBV infection or without immunity to HBV (anti-HBs <10 IU/mL)
- Patients with isolated anti-HBc .Recommend 1-time dose followed by anti-HBs at 1-2 months. If the titer is >100 IU/mL, no further vaccination is needed, but if the titer is <100 IU/mL, a complete series of HBV vaccine (single-dose or double-dose) should be completed followed by anti-HBs testing .
- Early vaccination is recommended before CD4 count falls below 350 cells/mm3 ,as low CD4 count at time of vaccination has been associated with poor response to the vaccine.
- However, in a patient with low baseline CD4 cell count, vaccination should not be deferred until CD4 reaches >350 cells/mm3, as some patients with CD4 <200 cells/mm3 do respond to vaccination .

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Preventing Recurrence

- As previously indicated, most patients should continue HBV therapy (with the exception of pegylated IFN) indefinitely because relapses after response occur, particularly in those with lower CD4 cell counts, and because reports of hepatitis flares after discontinuation of HBV-active drugs.

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