Hepatitis B Coinfection

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Module 4: Co-Occurring Conditions
Lesson 5: Hepatitis B Coinfection

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Background

Epidemiology

Hepatitis B virus (HBV) is a significant cause of liver disease among persons with HIV. For individuals with HIV who were born in the United States, acquisition of HBV occurs primarily through injection drug use and sexual contact, with most HBV infections occurring in adulthood.[1,2] Foreign-born persons, however, are likely to have acquired HBV earlier (at birth or in childhood). Genotypes A-J for HBV are geographically distributed, with genotype A as the predominant subtype in the United States among non-Asian people and genotype B or C among Asian people.[2,3,4] In the HIV Outpatient Study (HOPS) during the years 1996 through 2007, investigators reported 8.4% of persons with HIV tested positive for chronic HBV (either HBsAg-positive or HBV DNA positive), a prevalence 20-fold higher than the 0.42% prevalence in the general population (Figure 1).[5] In this same study, they reported the highest rate of chronic HBV was among men who have sex with men.[5] A separate review estimated an overall HBV prevalence of 6 to 14% among individuals with HIV in Western Europe and the United States, with prevalence rates of 4 to 6% in heterosexuals, 7 to 10% in people who inject drugs, and 9 to 17% in men who have sex with men (MSM).[6]

Impact of HIV and HBV Coinfection

When compared to individuals with HBV monoinfection, those with HBV and HIV coinfection have higher baseline HBV DNA levels, lower alanine aminotransferase (ALT) levels, and decreased rates of spontaneous hepatitis B e antigen (HBeAg) seroconversion.[7] Individuals with HBV and HIV coinfection have an accelerated progression of liver disease, as well as an increased risk of hepatocellular carcinoma, all-cause mortality, and liver-related mortality compared to persons with HIV monoinfection.[8,9,10,11] Among those with HIV and HBV coinfection, the highest liver-related mortality rates have occurred in individuals with low CD4 cell counts.[12] Multiple other studies have reported HIV and HBV coinfection and HIV and HCV coinfection have both played a major role in liver-related deaths in persons with HIV.[13,14,15,16,17] Further, a large observational cohort study from the United Kingdom reported increased liver-related mortality in persons who had coinfection with either HBV or HCV when compared with HIV monoinfection, but the highest liver-related mortality was seen in those with triple HIV-HCB-HCV infection (Figure 2).[18] The impact of HBV on the natural history of HIV remains less clear, with some studies demonstrating no significant effect of HBV coinfection on HIV-related outcomes and others suggesting an adverse impact.[19,20,21]

Immunization to Prevent Hepatitis B Infection

Although HBV vaccination has been recommended since the 1980s for men who have sex with men (as well as for persons who inject drugs and for heterosexuals with multiple sex partners), and since 2006 for all

individuals with HIV, HBV vaccination rates for persons with HIV remain low.[5,22,23,24] Indeed, recent surveillance data from the Centers for Disease Control and Prevention (CDC) suggest that over a third of the persons living with HIV who were receiving medical care in the United States did not have documentation of HBV infection, immunity, or vaccination.[25] Recommendations and vaccine schedules for HBV are addressed in detail in the Immunizations in Adults lesson in the Module Basic Primary Care.

Screening for HBV in Persons with HIV

Recommendations for Testing

All persons with HIV should undergo initial screening for HBV infection upon entry into medical care with a panel that consists of hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (HBsAb), and hepatitis B core antibody (anti-HBc total).[2] Chronic HBV infection is defined by the detection of HBsAg on two separate tests that have been obtained at least 6 months apart.[2] Thus, for persons who test positive for HBsAg, a repeat HBsAg test should be performed 6 months following this initial positive HBsAg to confirm that chronic HBV infection is present. Individuals with confirmed chronic HBV should have further testing that includes hepatitis B e antigen (HBeAg), antibody to HBeAg (anti-HBe), and HBV DNA.[2] In addition, for persons with HIV who have negative HBsAg testing, HBV DNA testing should be considered if they have persistent elevation in alanine aminotransferase levels (ALT) or they have suspected acute HBV infection and are in the serologic window period (loss of HBsAg without emergence yet of HBsAb).[26]

Interpretation of Hepatitis B Serologic Studies

Serologic testing for the diagnosis of HBV infection involves measurement of the full panel of distinct HBV-specific antigens and antibodies outlined above. Results of this serologic panel can help determine whether a patient is susceptible to infection, immune as a result of resolved infection, immune as a result of vaccination, acutely infected, or chronically infected (Figure 3).[24,27]

Laboratory Markers Following Acute HBV Infection

In persons with acute HBV infection, HBsAg can be detected in serum 4 to 10 weeks after HBV acquisition.[28] Although HBV DNA is usually detectable 10 to 20 days before the appearance of HBsAg, testing for HBV DNA is not part of routine HBV screening. Shortly after the appearance of HBsAg, HBeAg becomes evident; HBeAg is a marker of active viral replication, and persons with positive HBeAg typically have high levels of circulating serum HBV DNA.[29] Concurrent with the onset of clinical symptoms, anti-HBc appears, primarily detectable as the IgM class (IgM anti-HBc). Although IgM anti-HBc antibodies typically decline to undetectable levels within 6 months, the IgG class (IgG anti-HBc) persists indefinitely as a marker of past HBV infection. Resolution of infection is marked by the loss of HBsAg and the appearance of HBsAb. Individuals who clear HBV infection will also lose HBeAg and develop anti-HBe. It is important to note that for individuals who have cleared past infection, the epigenetic covalently closed circular (CCC) DNA persists in hepatocyte nuclei and remains the main barrier to true viral eradication or cure. Thus, individuals with prior clearance remain at risk of reactivation of HBV patients if they have severe immunosuppression, they are receiving immunosuppressive therapy (particularly B-lymphocyte-depleting treatments), or they are receiving direct-acting antiviral therapy for the treatment of hepatitis C virus.[30]

Isolated Hepatitis B Core Antibody

Among persons with HIV who undergo serologic testing for HBV, an estimated 17 to 41% have isolated anti-HBc.[31,32] There are four possible interpretations of this finding: (1) resolved HBV infection with waning HBsAb titers (most common), (2) a false-positive anti-HBc test, (3) occult "low-level" chronic HBV infection, or (4) resolving acute HBV infection.[27] For persons with HIV and isolated anti-HBc, the Adult and Adolescent OI Guidelines recommend the following approach (Figure 4).[2] This approach is based on findings from the NRS HB EP03 CISOVAC Prospective Study.[33,34]

- Administer a one-time standard dose of hepatitis B vaccine and check anti-HBs 1 to 2 months later.
    - If the anti-HBs titer is greater than 100 IU/mL, then no further vaccination is required. Note that the cut-off value of 100 IU/mL used in this setting is higher than the usual cutoff of 10 IU/mL to document immunity following routine immunization with hepatitis B vaccine.
    - If the anti-HBs titer is less than 100 IU/mL, then a complete series of HBV vaccine should be

completed, followed by anti-HBs testing 1 to 2 months after completing the series.

Screening Before Initiating NRTI-Sparing or NRTI-Limited Antiretroviral Regimens

The importance of HBV screening is essential when starting or switching a nucleoside reverse transcriptase inhibitor (NRTI)-limited or NRTI-sparing antiretroviral regimen, including dolutegravir-lamivudine, dolutegravir-rilpivirine, and injectable cabotegravir plus rilpivirine, since these regimens do not provide adequate treatment for HBV.[35] In addition, the antiretroviral regimen dolutegravir-abacavir-lamviudine does onto provide adequate treatment of HBV. Screening for HBV is this setting can identify (1) persons with chronic HBV who may not be a good candidate to receive a regimen that does not have adequate HBV treatment (or who would need additional HBV treatment if they switch to that regimen), (2) persons without protective HBV immunity who can benefit from HBV vaccination, and (3) persons with prior HBV infection who will need monitoring if they start on a NRTI-sparing or NRTI-limited regimen. The following factors should be taken into account:

- Persons with chronic HIV and HBV coinfection should, in general, avoid treatment with an antiretroviral regimen, such as dolutegravir-lamivudine, dolutegravir-rilpivirine, injectable cabotegravir plus rilpivirine, or dolutegravir-abacavir-lamivudine, that does contain two agents with strong HBV activity.
- If a NRTI-limited or NRTI-sparing regimen (e.g., dolutegravir-lamivudine, dolutegravir-rilpivirine. or injectable cabotegravir plus rilpivirine) is used in a person with HIV and HBV coinfection, then tenofovir DF, tenofovir alafenamide, or entecavir should be added. If there has been prior exposure to lamivudine monotherapy, then tenofovir DF or tenofovir alafenamide is preferred over entecavir due to the increased risk of HBV resistance to entecavir.
- People who have had prior HBV infection (indicated by negative HBsAg, positive anti-HBc, and either positive or negative anti-HBs) have less than 1% risk of HBV reactivation, and an even lower risk of HBV reactivation hepatitis. Among this group, people with positive HBsAb have the lowest risk of reactivation, though reactivation can occur if HBV-active therapy is discontinued as part of their antreitroviral regimen.[35,36]
- For those with prior HBV exposure but without active HBV infection, the antiretroviral guidelines suggest ALT monitoring every 1 to 3 months for 6 months after switching to a NRTI-sparing or NRTI-limited regimen. If there is an increase in ALT levels, HBV DNA testing is warranted to check for HBV reactivation hepatitis.[35]

Initial Evaluation of Persons with HBV and HIV Coinfection

Individuals with HIV who are also diagnosed with chronic HBV (positive HBsAg on two occasions at least 6 months apart) should undergo further HBV-related evaluation and receive counseling. The following information summarizes key recommendations for the initial evaluation of persons diagnosed with HBV in the setting of HIV coinfection:[2]

- **Baseline HBV DNA Level:** A quantitative HBV DNA level, in conjunction with serum ALT, provides key information that can help determine whether the patient has active infection. In persons with HBV monoinfection, the baseline HBV DNA level has also been shown to predict subsequent risk for cirrhosis and liver cancer.[37,38] If the person with HIV is already receiving HIV antiretroviral therapy with agents that have activity against HBV (e.g., tenofovir alafenamide, tenofovir DF, emtricitabine, and lamivudine), the HBV DNA level may be undetectable.
- **HBeAg and anti-HBe**: Baseline testing should include HBeAg and anti-HBe. HBeAg status helps determine the stage (phase) of HBV infection; loss of HBeAg associated with anti-HBe seroconversion is an important benchmark of therapy.
- **HBV Genotype and Baseline Resistance Assay**: Routine baseline HBV genotyping and resistance testing are not recommended.
- **Serologic Studies for Hepatitis A Virus (HAV) and HCV:** (1) Assess for HCV coinfection with HCV antibody and (2) determine immunity to HAV with HAV antibody (IgG or total). Persons without immunity to HAV should receive the HAV vaccine series. Persons with HBV and HCV coinfection have accelerated progression of liver fibrosis and, therefore, should receive HCV treatment as soon as possible.
- **Studies for Hepatitis D virus (HDV)**: In the United Sates, approximately 4% of individuals with HIV and HBV coinfection also have a positive HDV serologic test.[39] Hepatitis D virus is a small, defective virus that requires the presence of HBV to be able to complete its life cycle and propagate. Therefore, HDV can only persist in people who have active HBV infection. Individuals with a positive HDV serologic test should have testing for HDV RNA.[35]
- **Basic Evaluation and Monitoring of Liver Activity and Function:** Evaluate the individual's liver disease severity with platelet count, albumin, bilirubin, alkaline phosphatase, and prothrombin time, and hepatitis activity with ALT, aspartate aminotransferase (AST) at baseline and every 6 months.
- **Staging of Liver Fibrosis:** Consider noninvasive methods of staging, such as Aspartate aminotransferase-to-Platelet Ratio Index (APRI), Fibrosis-4 (Fib-4) Index, FibroTest (FibroSURE), and transient elastography (FibroScan) to assess for liver fibrosis.[40] Note that FibroTest and transient elastography have not been validated for use in clinical decision-making for patients with chronic HBV, with or without HIV.
- **Counseling**: Initial counseling should include the recommendation to (1) abstain from alcohol and (2) use effective methods to prevent secondary HBV transmission. These include the use of consistent barrier protection with sex partners, as well as testing and vaccination of susceptible partners and household members.

Treatment of HBV and HIV in Persons with HIV and HBV Coinfection

Goals for HBV Treatment in Persons with HIV Coinfection

The short-term goals for treating HBV in persons with HIV coinfection are the same as in persons with HBV monoinfection: normalize ALT levels, obtain HBeAg seroconversion (if HBe-antigen positive at baseline), and maintain suppression of HBV replication.[41] The long-term goals of HBV treatment are to halt or reverse fibrosis progression, reduce the risk of hepatic decompensation, prevent the development of hepatocellular carcinoma, and decrease HBV-associated mortality.[10,41,42] Data from persons with HBV monoinfection suggest HBV therapy can achieve these goals, but similar long-term studies in persons with HIV and HBV coinfection have not been published.[10,43] Nevertheless, cohort studies with at least a few years of follow-up time suggest that antiviral therapy can readily achieve the shorter-term goals of virologic suppression, HBeAg seroconversion, and even HBsAg seroconversion in persons with HIV and HBV coinfection [44,45,46].

General Approach

The Adult and Adolescent ART Guidelines recommend initiation of HIV antiretroviral therapy in all persons with HIV (regardless of CD4 cell count) to reduce the risk of disease progression and to prevent transmission of HIV.[47] For persons with HIV and HBV coinfection, the treatment should consist of a regimen that provides maximum suppression of both HIV and HBV, regardless of baseline CD4 cell count or HBV DNA levels.[35] Specifically, the antiretroviral regimen should include two agents that have full activity against HBV. Among the HIV antiretroviral medications, four nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs)—tenofovir alafenamide, tenofovir DF, emtricitabine, and lamivudine—also have antiviral activity against HBV. Although emtricitabine and lamivudine can be used interchangeably, they should not be used together and neither provide adequate treatment of HBV when used alone. Tenofovir alafenamide and tenofovir DF are both highly active against HBV, have a high genetic barrier for development of HBV drug resistance, and are active against lamivudine- or emtricitabine-resistant HBV variants.[35,48] Note, there are now multiple 2-drug antiretroviral regimens that do not have adequate activity to effectively treat HBV, including dolutegravir-rilpivirine, injectable cabotegravir and rilpivirine, and dolutegravir-lamivudine. In addition, the recommended 3-drug antiretroviral regime dolutegravir-abacavir-lamivudine also does not have adequate activity to effectively treat HBV.

HIV and HBV Coinfection Treatment Data

Antiretroviral regimens that include dual combination of either tenofovir DF-emtricitabine or tenofovir DF plus lamivudine have been shown to be highly efficacious in suppressing HBV DNA levels in persons with HIV and HBV coinfection.[45,49,50,51,52] In addition, tenofovir DF has been shown to suppress HBV DNA levels in persons with lamivudine-resistant HBV.[53,54,55] There are, however, less extensive data on HBV treatment efficacy of tenofovir alafenamide in persons with HIV and HBV coinfection. Two phase 3 trials in adults with chronic HBV monoinfection have demonstrated comparable efficacy of a 25 mg once-daily dose of tenofovir alafenamide (compared with tenofovir DF) for the treatment of HBV monoinfection, including one study in HBeAg-negative adults and one in HBeAg-positive participants.[56,57] Another trial involving persons with HBV monoinfection demonstrated that a switch from tenofovir DF to tenofovir alafenamide did not result in a reduction in efficacy for HBV treatment.[58] In an open-label, non-comparative switch trial in persons with HIV and HBV coinfection, investigators evaluated the efficacy of switching patients to elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine and after 48 weeks, 66 (92%) of patients maintained or achieved virologic suppression of both viruses (HIV RNA level less than 50 copies/mL and HBV DNA less than 29 IU/mL).[59]

Recommended Treatment of HIV and HBV Coinfection

When treating persons with HIV and HBV coinfection, the Adult and Adolescent ART Guidelines recommend using an antiretroviral regimen that includes a nucleoside/nucleotide reverse transcriptase inhibitor backbone

of either tenofovir alafenamide-emtricitabine, tenofovir DF-emtricitabine, or tenofovir DF-lamivudine as part of a fully suppressive regimen.[2,35] Since tenofovir alafenamide-emtricitabine and tenofovir DF-emtricitabine are commonly used as the backbone NRTIs in most recommended HIV antiretroviral regimens for initial therapy, concomitant treatment of HIV and HBV can be achieved in nearly all circumstances without having to make special adjustments in the antiretroviral regimen.[2,35,47] Note that the regimens dolutegravir-abacavir-lamivudine and dolutegravir-lamivudine are not recommended as initial therapy in persons with HIV and HBV coinfection.[35,47]

Table 1. **Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV**

Recommended Initial Regimens for People with HIV and HBV Coinfection

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use. Choice of antiretroviral therapy during pregnancy should be guided by recommendations from the Perinatal Guidelines.
For people who do NOT have a history of long-acting cabotegravir use as HIV PrEP, the following regimens are recommended:
INTI + 2 NRTIs: • Bictegravir-tenofovir alafenamide-emtricitabine (AI) • Dolutegravir plus (tenofovir alafenamide or tenofovir DF)[a] plus (emtricitabine or lamivudine) (AI)
For people with HIV and a history of using long-acting cabotegravir as HIV PrEP, integrase genotypic drug resistance testing should be done before the start of antiretroviral therapy. If treatment is begun prior to the results of genotypic testing, the following regimen is recommended:
Boosted PI + 2 NRTIs: • Darunavir (boosted with cobicistat or ritonavir) plus (tenofovir alafenamide or tenofovir DF) plus (emtricitabine or lamivudine)—pending the results of the genotype test (AIII).
Abbreviations: HBV = hepatitis B virus; INSTI = integrase strand transfer inhibitor; NRTI = nucleoside reverse transcriptase inhibitor [a]Tenofovir alafenamide and tenofovir DF are two forms of tenofovir approved by the FDA. Tenofovir alafenamide has fewer bone and kidney toxicities than tenofovir DF, whereas tenofovir DF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs. Rating of Recommendations: A = Strong; B = Moderate; C = Optional Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion

Source:

- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents HIV. Department of Health and Human Services. Considerations for antiretroviral use in patients with coinfections: hepatitis B virus/HIV coinfection. September 12, 2024. [HIV.gov]

- **Preferred Therapy with CrCl 60 mL/min or Greater**: The antiretroviral regimen must include two drugs active against HBV, preferably with one of the following oral regimens: (1) tenofovir alafenamide 25 mg plus emtricitabine 200 mg once daily, (2) tenofovir DF 300 mg plus emtricitabine 200 mg, or (3) tenofovir DF 300 mg plus lamivudine 300 mg. Note the dose of tenofovir alafenamide is 10 mg when used as a component of a single-tablet regimen that also contains cobicistat (elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine and darunavir-cobicistat-tenofovir alafenamide-emtricitabine).
- **Alternative Therapy**: If neither tenofovir alafenamide nor tenofovir DF can be used, then entecavir should be added to a fully suppressive HIV antiretroviral regimen that includes lamivudine or emtricitabine; this addition of entecavir, which is not used to treat HIV, provides a second agent active against HBV.[2,35] For persons with known or suspected lamivudine-resistant HBV, the once-daily oral dose of entecavir should be increased from 0.5 mg to 1.0 mg with normal renal function; entecavir requires dose reduction if the CrCl is less than 50 mL/min).[2,35,41,60]
- **Therapies Not Recommended**: For individuals with HIV and HBV coinfection, the use of lamivudine or emtricitabine without tenofovir alafenamide, tenofovir DF, or entecavir should be avoided since monotherapy of HBV with lamivudine or emtricitabine is associated with high cumulative rates of HBV virologic failure and emergence of resistance (Figure 5).[2,61,62] In addition, regimens that contain adefovir are not recommended in persons with HBV and HIV coinfection due to inferior antiviral activity compared with tenofovir alafenamide or tenofovir DF.[2] Last, peginterferon is not recommended for HBV treatment in people with HIV and HBV coinfection due to treatment-associated toxicities.[35]

Recommended Regimens with Reduced Renal Function

- **Preferred Therapy with CrCl 30 to 59 mL/min**: Since the antiretroviral regimen should include two drugs active against HBV, the best option with mild renal impairment is tenofovir alafenamide 25 mg plus emtricitabine 200 mg PO once daily. Note the dose of tenofovir alafenamide is 10 mg when used as a component of a single-tablet regimen that also contains cobicistat (e.g., elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine and darunavir-cobicistat-tenofovir alafenamide-emtricitabine).
- **Preferred Therapy with CrCl Less than 30 mL/min**: Two options can be considered: (1) Use a fully suppressive antiretroviral regimen without tenofovir alafenamide or tenofovir DF and add renal-dosed entecavir to the regimen, or (2) use antiretroviral therapy with adjusted renal dosing of tenofovir DF and emtricitabine (when recovery of renal function is unlikely for patients with renal impairment). There is a tenofovir alafenamide 25 mg tablet (not combined with emtricitabine) that is FDA-approved for the treatment of HBV monoinfection, and it could be used for persons with a CrCl of 15 mL/min or greater and in persons on hemodialysis. In persons with a CrCl between 15 and 30 mL/min, it would therefore be possible to use tenofovir 25 mg daily combined with renal-dosed lamivudine (150 mg first dose, then 100 mg daily).

Caution and Contraindications

All antivirals with activity against HBV can potentially cause lactic acidosis and should be used with caution in persons with impaired hepatic function, especially with a Model for End-Stage Liver Disease (MELD) score greater than 18.[63] However, in a phase 2 study comparing tenofovir DF, tenofovir DF-emtricitabine, and entecavir, all regimens were well tolerated in persons with decompensated chronic HBV-associated liver disease, and it is unclear which is the best option for these individuals.[64] In addition, interferon (pegylated

or standard) is contraindicated for use in persons with decompensated (Child-Turcotte-Pugh class B or C) liver disease, due to the risk of hepatic decompensation with interferon-based therapy.[2]

Monitoring HBV Treatment Response

Monitoring Response to HBV Treatment

Monitoring the virologic response to HBV therapy should consist of checking HBV DNA levels every 3 to 6 months.[2] The HBV DNA levels accurately predict response to therapy, and regular monitoring during therapy is recommended to prevent or minimize the development of drug-resistant variants. In addition, for those individuals who are HBeAg-positive at baseline, testing for HBeAg every 6 months is recommended after the person achieves HBV viral suppression. The decline to an undetectable HBV DNA level typically takes longer than the time to undetectable HIV RNA in response to antiretroviral therapy; an incompletely suppressed HBV DNA level after 24 weeks often occurs with HBV therapy, particularly if the baseline level exceeds 100,000 IU/mL. Once the HBV levels become undetectable, the frequency of monitoring HBV DNA levels can change to every 6 months.

Definitions of Treatment Response

The Adult and Adolescent OI Guidelines provide the following definitions for the different virologic responses, based on those generated by the European Association for the Study of the Liver (EASL) (Figure 12).[2]

- **Primary Virologic Nonresponse**: less than 1 $\log_{10}$ IU/mL decline in HBV DNA levels 12 weeks after starting therapy
- **Partial Virologic Response**: greater than or equal to 1 $\log_{10}$ IU/mL decline in HBV DNA levels at 24 weeks, but HBV DNA remains detectable
- **Complete Virologic Response**: undetectable HBV DNA levels at 24 to 48 weeks using a real-time HBV DNA assay
- **Maintained Virologic Response**: complete virologic response that continues while the individual is on therapy for HBV
- **Sustained Virologic Response:**a virologic response that is still present 6 months after discontinuing therapy

Monitoring for Medication-Related Toxicity

The Adult and Adolescent OI Guidelines also highlight the additional risks conferred by the use of specific anti-HBV medications and recommend the following additional monitoring strategies.[2]

- **Tenofovir DF and Tenofovir Alafenamide**: Similar to patients with HIV monoinfection who take tenofovir DF, persons with HIV and HBV coinfection should have electrolytes and serum creatinine checked every 3 to 6 months and urinalysis every 6 months. For persons with a GFR of 30 to 59 mL/min, the tenofovir alafenamide-emtricitabine regimen is preferred.[2] Tenofovir alafenamide-emtricitabine is not FDA-approved for use when the CrCl is less than 30 mL/min, but tenofovir alafenamide alone, which is FDA-approved for the treatment of HBV, is approved for use in patients with a CrCl of 15 mL/min or greater.[65]
- **HIV Antiretroviral Therapy**: When using modern antiretroviral regimens to treat HIV, antiretroviral medication-related liver toxicity is uncommon. With current antiretroviral agents, an increase in aminotransferase levels that occurs in a patient with HBV coinfection who recently started on HIV antiretroviral therapy would most likely be a result of HBV-related immune reconstitution inflammation.[66]

Management of HIV or HBV Virologic Failure

Management of HIV Virologic Failure

If an individual with HIV and HBV coinfection experiences HIV virologic failure, but continues to have adequate HBV suppression on the regimen, then the antiretroviral medications that are active against HBV should be continued (assuming the person is tolerating these medications) and given in combination with additional antiretroviral medications that are chosen based on HIV drug resistance genotypic testing.[2]

Management of Hepatitis B Treatment Failure

For the purposes of management, HBV treatment failure should be categorized as follows: (1) primary nonresponse after 12 weeks of therapy (less than 1 $\log_{10}$ decline in HBV DNA levels) or (2) an increase in HBV DNA of greater than 1 $\log_{10}$ above nadir.[2] It is important to recognize that HBV DNA levels may decline very slowly, especially in the setting of high pretreatment DNA levels and low CD4 cell counts, with some individuals taking a few years or more to completely suppress HBV DNA.[45,67] These slow kinetics in HBV DNA level decreases are not necessarily associated with HBV drug resistance,[68,69] but when lamivudine or emtricitabine is used without another active agent against HBV, resistance frequently develops.[2,61,62] The Adult and Adolescent OI Guidelines recommend the following strategies for the management of HBV treatment failure in persons with HIV coinfection.[2]

- Because of the high rates of resistance to lamivudine (or emtricitabine) monotherapy to treat hepatitis B, these agents should not be used as the only agent active against HBV.[2,35] If a person has been receiving lamivudine (or emtricitabine) as the sole agent against HBV, then tenofovir DF or tenofovir alafenamide should be added.[2,35] This strategy should be used even if lamivudine (or emtricitabine) HBV drug resistance is not suspected or documented.
- Because tenofovir has a high genetic barrier to HBV resistance, the development of HBV drug resistance to tenofovir alafenamide or tenofovir DF is uncommon.[70] Therefore, it is reasonable to continue tenofovir alafenamide or tenofovir DF in the setting of slowly declining HBV DNA levels, along with close monitoring.[48,70,71,72]
- Because entecavir resistance can emerge more readily in persons with preexisting lamivudine resistance, entecavir is not generally recommended as the mainstay of HBV therapy in such individuals. If it is necessary to use entecavir in that setting, use of higher-dose entecavir (1.0 mg/day rather than 0.5 mg/day) and more frequent monitoring of HBV DNA levels is recommended.[2]
- If treatment failure occurs on entecavir, then the best alternative is to use tenofovir DF with or without emtricitabine (since entecavir resistance confers cross-resistance with emtricitabine, lamivudine, and telbivudine).[2]
- Drug resistance is not generally encountered with interferon-based therapy. If, however, treatment failure occurs on peginterferon, the HBV treatment regimen can be switched to oral nucleoside/nucleotide analog therapy; this change will require coordination with the existing HIV antiretroviral regimen.

Stopping HBV Treatment and Hepatic Flares

In persons receiving treatment with one or more antiviral agent(s) active against HBV, stopping therapy may result in HBV reactivation and potentially serious hepatic inflammation, which is marked by a rise of serum hepatic aminotransferase levels and commonly referred to as a hepatic flare—defined as an ALT increase to at least 3 times greater than the baseline level or ALT greater than 100 U/L.[30] In one study involving 255 individuals with HIV and HBV coinfection, when lamivudine was discontinued, approximately 30% of the participants had increases in ALT levels, 5% had grade 3 or grade 4 elevations, and approximately 1% developed fulminant hepatitis and hepatic decompensation (Figure 13).[73] If a hepatic flare occurs after stopping antiviral therapy, the onset is typically within 6 months after cessation of therapy.[74]

Management of Hepatic Flare

Individuals with HIV and HBV coinfection who stop antiviral therapy should have monitoring of aminotransferase levels every 6 weeks for 3 months and then every 3 months thereafter.[2] If a flare develops after stopping HBV therapy, the appropriate course of management is to restart antiviral therapy using a regimen that is fully suppressive for both HIV and HBV. It is also important to note that persons with HIV and HBV coinfection who abruptly stop antiretroviral therapy can have an abrupt marked increase in HIV RNA levels and develop a clinical illness similar to that observed in persons with acute HIV.[75]

HBV-Related Immune Reconstitution Syndrome (HBV-IRIS)

In persons with HIV and HBV coinfection, hepatic inflammation can occur after immune recovery in response to effective HIV antiretroviral therapy. This clinical scenario is commonly referred to as immune reconstitution inflammatory syndrome (IRIS).

Risk Factors for Developing HBV-Related IRIS

Although the risk of HBV-related IRIS is highest if HIV is treated without effective therapy against HBV, it can occur even with regimens that are fully active against both HIV and HBV.[76,77] Baseline risk factors (prior to initiation of antiretroviral therapy) associated with HBV-related IRIS include low CD4 cell count, high HBV DNA level, and elevated baseline ALT level.[78]

Timing and Differential Diagnosis with HBV-Related IRIS

The hepatitis flare is first detected as an increase in ALT levels, typically within 3 to 12 weeks after starting antiretroviral therapy. The differential diagnosis includes direct drug or alcohol hepatotoxicity, a new viral hepatitis infection (acute hepatitis A or C), or an opportunistic infection. To help distinguish between these conditions, a review of the medication history, prior hepatitis A immunization, and history of recent HCV exposure would be indicated, as well as measurement of serum HBV DNA, HIV RNA, and CD4 cell count.[2]

Monitoring for HBV-Related IRIS

Recommended monitoring for HBV-related IRIS consists of checking ALT levels monthly for 3 to 6 months after initiating antiretroviral therapy, then every 3 months thereafter.[2] If, at 12 months after starting antiretroviral therapy, IRIS has not developed, it is reasonable to return to routine laboratory monitoring.

Management of HBV-Related IRIS

For individuals who develop HBV-related IRIS (as indicated by rising ALT levels in the setting of immune recovery), existing guidelines recommend continuing therapy for HIV and HBV, unless the individual develops drug-induced hypersensitivity (e.g., Stevens Johnson Syndrome or Drug Reaction with Eosinophilia and Systemic Symptoms [DRESS]), symptomatic hepatitis (nausea, vomiting, abdominal pain, or jaundice), or the ALT increases to greater than 10 times the upper limit of normal.[2] With severe IRIS, particularly in a person with cirrhosis, consultation with a hepatologist is recommended.[2] Although corticosteroids are used to manage some IRIS-related disorders, there are insufficient data to recommend for or against the use of corticosteroids in an individual with HIV who has hepatitis B-related IRIS.[2]

Hepatitis D Virus

Hepatitis D virus (HDV), formerly hepatitis delta virus, is a defective satellite RNA virus that depends on the HBsAg for the encapsulation of the HDV genome—it cannot exist or infect individuals in the absence of active HBV infection. The rate of triple infection with HIV, HBV, and hepatitis D virus is estimated to occur in about 4% of persons with HIV and HBV coinfection).[39,79,80] Among those with positive HIV, HBV, and HDV serology, approximately 40% have a positive HDV RNA test.[39] Although triple infection with HIV-HBV-HDV has no known adverse impact on clinical, virologic, or immunologic responses to antiretroviral therapy when compared with dual HIV and HBV infection, it may accelerate progression of liver fibrosis, increase the risk of liver cirrhosis, and elevate the likelihood of developing hepatocellular carcinoma.[79,81]

Treatment of Hepatitis D Virus

There are currently no treatment options specifically FDA-approved for the treatment of HDV, other than suppressing the HBV infection. Although peginterferon has been recommended as the mainstay of therapy for HDV, some data suggest tenofovir DF can lower HDV RNA levels in a subset of persons with HDV infection.[80,82] The suppression of HDV RNA levels with tenofovir DF is not reliably sustained, and, at this time, tenofovir DF is not considered the main treatment for HDV.[83] Individuals with HIV-HBV-HDV triple infection should have referral to a specialist who has expertise in this area.[35]

Preventing HBV Perinatal Transmission

Risk of HBV Perinatal Transmission

The overall rate of transmission of HBV from an HBsAg-positive woman to her neonate during the perinatal period can be as high as 90% in the absence of immunoprophylaxis. The presence of HBeAg and the associated higher HBV DNA levels mediate this risk: mothers with a positive HBeAg test have a perinatal transmission rate of 70 to 90%, whereas those with a negative HBeAg test have a rate of transmission less than 10%.[24,27] When perinatal transmission of HBV occurs, it usually happens during or shortly before delivery, but can take place less frequently in utero. The exact rate of perinatal HBV transmission among pregnant women with HIV and HBV coinfection is not well established. Transmission of HBV through breast milk is not a significant source of perinatal HBV transmission in an infant who has received appropriate immune prophylaxis.

Strategy for Preventing HBV Perinatal Transmission

In a pregnant woman with HIV and HBV coinfection, the following strategies should be used to effectively prevent the maternal-to-child transmission of HBV and HIV: (1) suppression of maternal HIV RNA and HBV DNA to undetectable levels during pregnancy and delivery and (2) administration of prophylaxis to the infant after birth (antiretroviral medication for HIV and immunoglobulin and HBV vaccine for HBV). For persons with HBV monoinfection, there is no contraindication to breastfeeding.[27,84] Therefore, decisions regarding breastfeeding should be based on shared decision-making regarding the risk of HIV transmission via breastfeeding.[85] The mode of delivery in pregnant women with HIV and HBV coinfection should be based on standard obstetrical and HIV-related indications, as there is no indication that cesarean section impacts the risk of vertical HBV transmission.[86,87] Women who are pregnant and have HIV and HBV coinfection, should receive hepatitis A virus vaccination during pregnancy if not already immune.

Antiviral Regimens for Pregnant Women with HBV and HIV Coinfection

Unfortunately, even with fully suppressed HBV DNA levels, the risk of HBV perinatal transmission is not completely eliminated.[88] Lamivudine, emtricitabine, and tenofovir DF have been studied in pregnancy and can be used safely.[41] According to the Perinatal HIV Clinical Guidelines, the preferred dual NRTI backbone of antepartum antiretroviral therapy for pregnant women with HIV and HBV coinfection is either (1) tenofovir DF-emtricitabine, (2) tenofovir DF plus lamivudine, or (3) tenofovir alafenamide-emtricitabine.[86] An additional third antiretroviral medication is needed to complete the regimen for HIV therapy, and this medication can be determined based on recommended HIV antiretroviral regimens for use during pregnancy.[89] Peginterferon alfa is an abortifacient at high doses and should not be used in pregnancy.[35]

HBV Prevention Measures for Neonates

Infants weighing greater than 2,000 grams who are born to persons with HBV infection, regardless of HBV treatment status during pregnancy, should receive one dose of hepatitis B immune globulin and the first dose of the HBV vaccine series within 12 hours of birth. The second and third doses of vaccine should be administered at 1 and 6 months of age, respectively.[2] Management of infants weighing less than 2,000 grams is the same, except that the initial vaccine dose (at birth) should not be counted as part of the vaccine series due to potentially lower immunogenicity in these infants; 3 additional doses of vaccine (for a total of 4 doses) should be administered beginning at age 1 month, then at age 2-3 months, and then again at age 6 months.[27] Postvaccination testing for both anti-HBs and HBsAg should be performed in all infants after completion of the vaccine series, at age 9 to 18 months (but not before 9 months of age or earlier than 4 weeks after the last vaccine dose); this regimen is greater than 95% effective in preventing HBV infection in these infants.[86]

Surveillance for Hepatocellular Carcinoma

Indications for Hepatocellular Carcinoma Surveillance

In persons with HIV and HBV coinfection, hepatocellular carcinoma usually develops at an earlier age and progresses faster than in persons with HBV monoinfection.[42,90] Data from populations with HBV monoinfection demonstrate an incidence of hepatocellular carcinoma in chronic HBV of about 0.5% of persons per year, and this rate increases to 2.5% per year in persons with cirrhosis.[91] For individuals who have evidence of cirrhosis, including those with HIV and HBV coinfection, screening for hepatocellular carcinoma is strongly recommended.[2,92] In general, persons diagnosed with hepatocellular carcinoma have a poor prognosis, but survival may be improved if the cancer is detected at a very early stage. There is one randomized, controlled trial as well as observational data to support HCC screening in people with chronic HBV infection, and while the evidence is not methodologically strong, HCC screening is now the standard of care.[93,94]

HCC Surveillance Recommendations for Persons with HIV and HBV Coinfection

For persons with HIV and HBV coinfection, hepatocellular carcinoma surveillance is indicated in the following groups.[2]

- All persons with cirrhosis, regardless of cause
- Asian men older than 40 years of age
- Asian women older than 50 years of age
- Men who are from sub-Saharan Africa and are older than 20 years of age
- Some experts recommend HCC surveillance for all persons with HIV and HBV coinfection who are older than 40 years of age:

HCC Surveillance Recommendations for Persons with HBV Monoinfection

For persons with HBV monoinfection, the 2023 American Association for the Study of Liver Diseases (AASLD) Guidance for Hepatocellular Carcinoma Surveillance provides slightly different recommendations than those for persons with HIV and HBV coinfection.[95] For persons with chronic HBV monoinfection (HBsAg positive), the AASLD recommends hepatocellular carcinoma surveillance for the following.[95]

- All persons with cirrhosis
- Man from endemic country older than 40 years of age
- Woman from endemic country older than 50 years of age
- Person from Africa at earlier age (can be initiated as early as third decade of life)
- Persons with a first-degree family member with a history of hepatocellular carcinoma
- PAGE-B score >10 (requires use of PAGE-B calculator)

HCC Surveillance after Clearance of HBsAg

For persons with chronic HBV infection who experience spontaneous or treatment-related clearance of HBsAg, the risk of developing liver disease progression declines considerably, as does the risk of hepatocellular carcinoma. The risk of hepatocellular carcinoma, however, is thought to persist, particularly in those who are older than 50 years of age and/or have cirrhosis. There are limited data on the natural history of persons with HIV who experience HBsAg clearance. Therefore, these individuals should continue to receive hepatocellular carcinoma surveillance.

Method of Hepatocellular Carcinoma Surveillance

The AASLD 2023 Guidance for HCC Surveillance recommends performing hepatic ultrasound and serum alpha-

fetoprotein (AFP), every 6 months for hepatocellular carcinoma surveillance.[95] The hepatocellular carcinoma surveillance methods are the same for persons with HIV and HBV coinfection as with HBV monoinfection.

Managing Persons with Coinfection and Advanced Liver Disease

The management of persons with HIV and HBV coinfection who develop cirrhosis and/or end-stage liver disease is the same as in patients with HBV monoinfection and involves close clinical monitoring.

- **Screening for Gastroesophageal Varices**: Patients with HBV and cirrhosis should undergo baseline screening with an esophagogastroduodenoscopy (EGD) to determine whether they have gastroesophageal varices large enough to warrant variceal bleed prophylactic therapy.[96] Patients with varices should undergo evaluation by a medical provider or specialist experienced with management of cirrhosis and prevention of variceal bleeding. If no substantial varices are observed, then EGD should be repeated every 2 years or sooner if liver decompensation occurs (progression from Child-Turcotte-Pugh Class A to Child-Turcotte-Pugh Class B/C cirrhosis).
- Liver Transplantation: Liver transplantation is not readily available for many patients with HIV, but has been shown to have favorable outcomes in persons with HIV and HBV coinfection.[97] The management of decompensated cirrhosis or end-stage liver disease in a person with HIV and HBV coinfection should be done by or under the guidance of a hepatologist.[2]

Summary Points

- In the United States, approximately 10% of persons with HIV have HBV coinfection; these individuals have a higher risk of liver-related morbidity and mortality when compared to those with HBV monoinfection. Persons with HIV and HBV coinfection should undergo screening for HDV.
- The long-term treatment goals are the same for persons with HIV and HBV coinfection as for those with HBV monoinfection: delay progression of liver disease, reduce the risk of hepatocellular carcinoma, and improve survival.
- The recommended antiretroviral regimens for treating persons with HIV and HBV coinfection should include three medications that are active against HIV and two medications that are active against HBV. The preferred regimens include tenofovir alafenamide-emtricitabine, tenofovir DF-emtricitabine, or tenofovir DF plus lamivudine as part of a fully suppressive antiretroviral regimen.
- Use of emtricitabine or lamivudine as the only agent active against HBV in an antiretroviral regimen should be avoided whenever possible, given the high rates of HBV resistance that develop with these medications.
- People with chronic HBV can have immune reconstitution syndrome with hepatic inflammation after initiating antiretroviral therapy.
- For persons with HIV and HBV coinfection and mild renal dysfunction, tenofovir alafenamide can be used as a substitute for tenofovir DF. Tenofovir alafenamide can also be used for those with severe renal dysfunction who are receiving hemodialysis.
- All people with HIV and HBV confection should receive immunization against HAV, unless they are already immune.
- Management of pregnant women with HIV and HBV coinfection requires antepartum, intrapartum, and postpartum interventions to reduce the risk of perinatal transmission of both HIV and HBV.
- All persons with chronic HBV infection, including those with HIV and HBV coinfection, should be evaluated for whether hepatocellular carcinoma surveillance is indicated.
- The management of women with HIV and HBV coinfection who develop cirrhosis and/or end-stage liver disease is generally the same as persons with HBV monoinfection and involves close clinical monitoring and the assistance of a hepatologist when indicated.

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Figures

Figure 1 Prevalence of Chronic Hepatitis B in Persons with HIV—HIV Outpatient Study, 1996-2007

These data are from the HIV Outpatient Study (HOPS), 1996-2007

Source: Spradling PR, Richardson JT, Buchacz K, Moorman AC, Brooks JT; HIV Outpatient Study (HOPS) Investigators. Prevalence of chronic hepatitis B virus infection among patients in the HIV Outpatient Study, 1996-2007. J Viral Hepat. 2010;17:879-86.

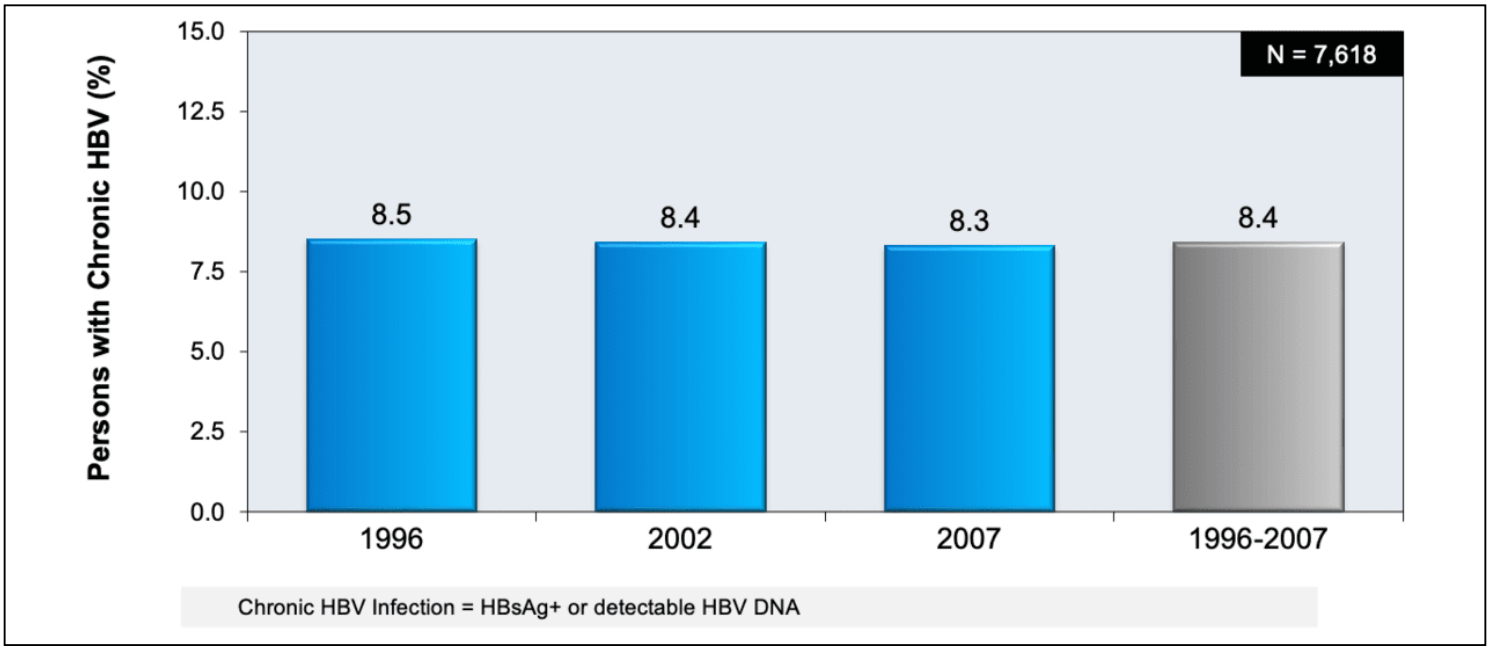

Figure 2 Liver-Related Mortality in Persons with HIV Based on HBV and HCV Coinfection Status, 2004–2012

These data are from 25 ,486 individuals enrolled in the UK Collaborative HIV Cohort (UK CHIC) study during the years 2004-2012. Coinfection with HBV or HCV increased liver-related mortality. The highest liver-related mortality was among those triple-infected with HIV, HBV, and HCV.

Source: Thornton AC, Jose S, Bhagani S, et al. Hepatitis B, hepatitis C, and mortality among HIV-positive individuals. AIDS. 2017;31:2525-32.

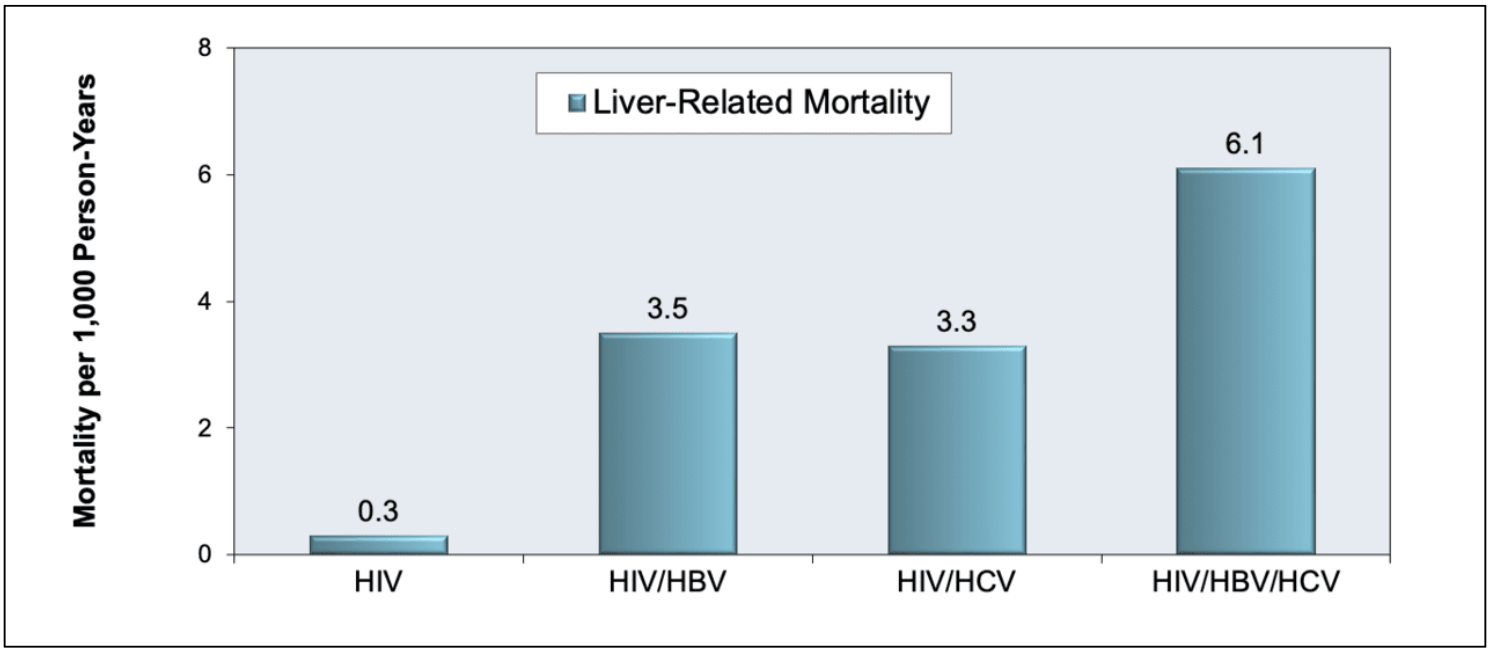

Figure 3 Interpretation Hepatitis B Serologic Test Results

Source: Mast EE, Margolis HS, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) part 1: immunization of infants, children, and adolescents. MMWR Recomm Rep. 2005;54:1-31.

Interpretation of Hepatitis B Serologic Test Results

HBsAg	Anti-HBc	IgM Anti-HBc	Anti-HBs	Interpretation
–	–	–	–	Susceptible to HBV infection
–	+	–	+	Immune due to natural hepatitis B infection
–	–	–	+	Immune due to hepatitis B vaccination
+	+	+	–	Acute HBV
+	+	–	–	Chronic hepatitis B infection
–	+	–	–	Interpretation unclear; four possibilities: 1. Resolved infection (most common) 2. False-positive anti-HBc, thus susceptible 3. “Low level” chronic infection 4. Resolving acute infection

Figure 4 Approach to Isolated Anti-HBc in Persons with HIV

Source: Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Hepatitis B virus infection. Last Updated: April 13, 2023.

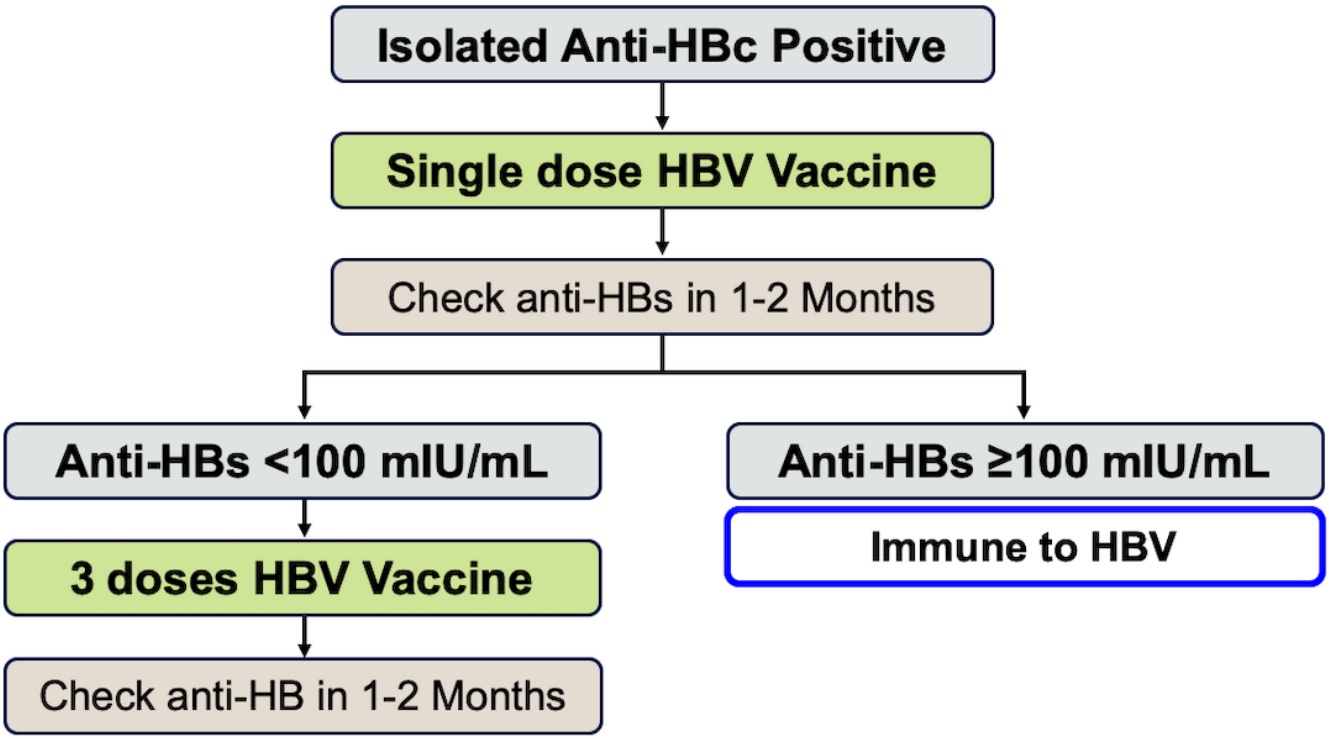

Figure 5 HBV Drug Resistance in Persons with HIV and Prolonged Lamivudine Use

The graphic shows the prevalence of HBV lamivudine-resistant mutations increased with longer duration of lamivudine therapy.

Source: Matthews GV, Bartholomeusz A, Locarnini S, et al. Characteristics of drug resistant HBV in an international collaborative study of HIV-HBV-infected individuals on extended lamivudine therapy. AIDS. 2006;20:863-70.

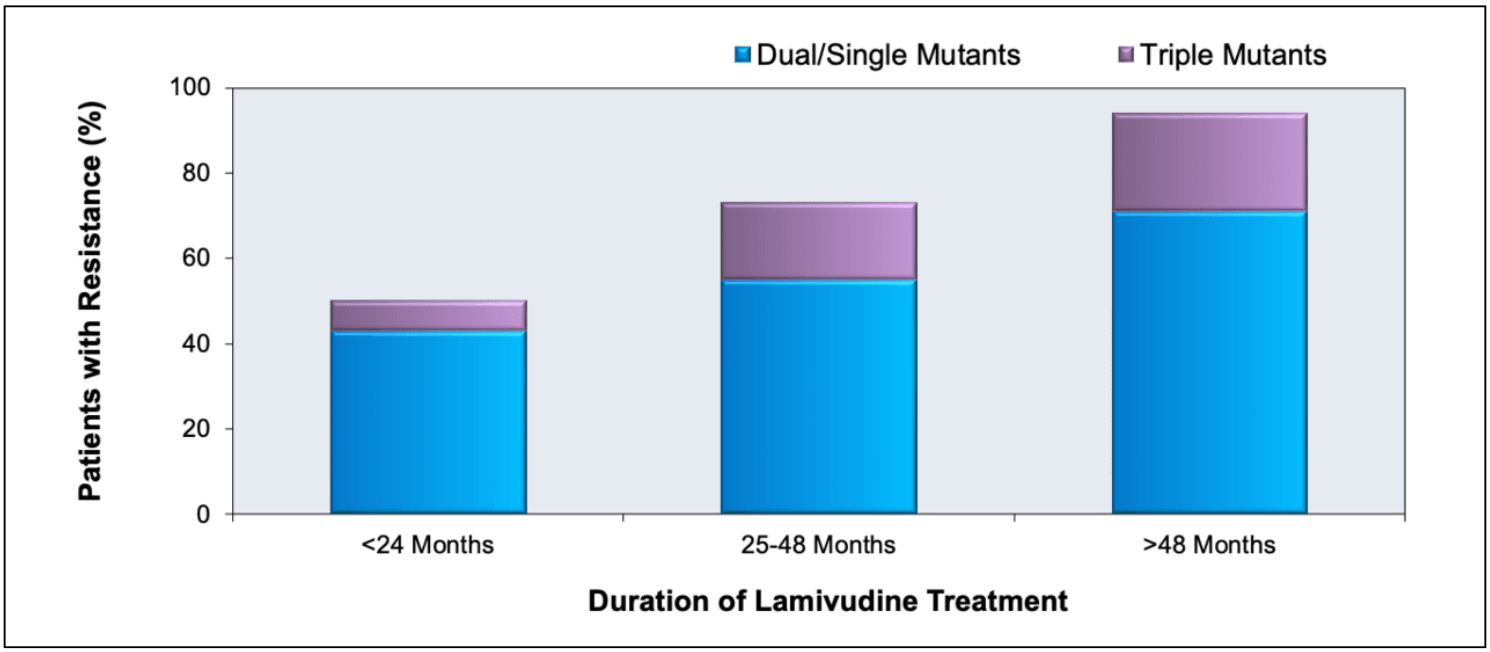

Figure 6 Antiviral Agents with Activity Against HBV and HIV

Note: in this table tenofovir includes tenofovir DF and tenofovir alafenamide.

Source: Iser DM, Sasadeusz JJ. Current treatment of HIV/hepatitis B virus coinfection. J Gastroenterol Hepatol. 2008;23:699-706.

Medication	HBV Activity	HIV Activity	Selection of HIV Resistance Reported
Lamivudine	Yes	Yes	Yes
Adefovir	Yes	No[a]	No
Entecavir	Yes	Partial	Yes
Emtricitabine	Yes	Yes	Yes
Telbivudine	Yes	Partial[b]	No
Tenofovir alafenamide	Yes	Yes	Yes
Tenofovir disoproxil fumarate	Yes	Yes	Yes

[a] = anti-HIV activity at higher doses; more potent against HBV
[b] = No in vitro activity observed against HIV, but HIV RNA decline reported

Figure 7 HBV Therapy: Primary Virologic Nonresponse

This graphic shows a less than 1 $\log_{10}$ IU/mL decline in HBV DNA levels 12 weeks after starting therapy

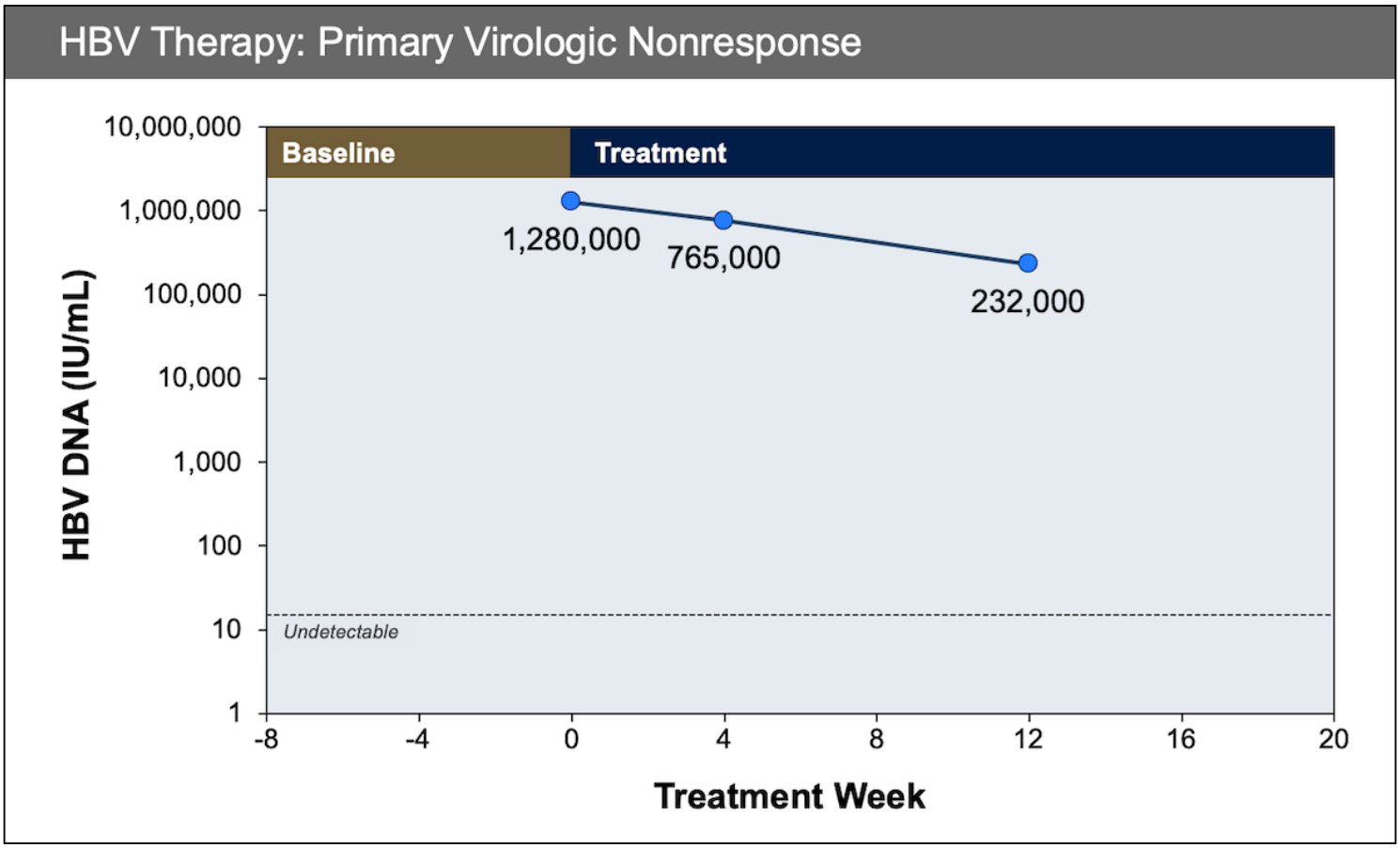

Figure 8 HBV Therapy: Partial Virologic Response

This graphic shows a greater than or equal to 1 $\log_{10}$ IU/mL decline in HBV DNA levels at 24 weeks, but HBV DNA remains detectable

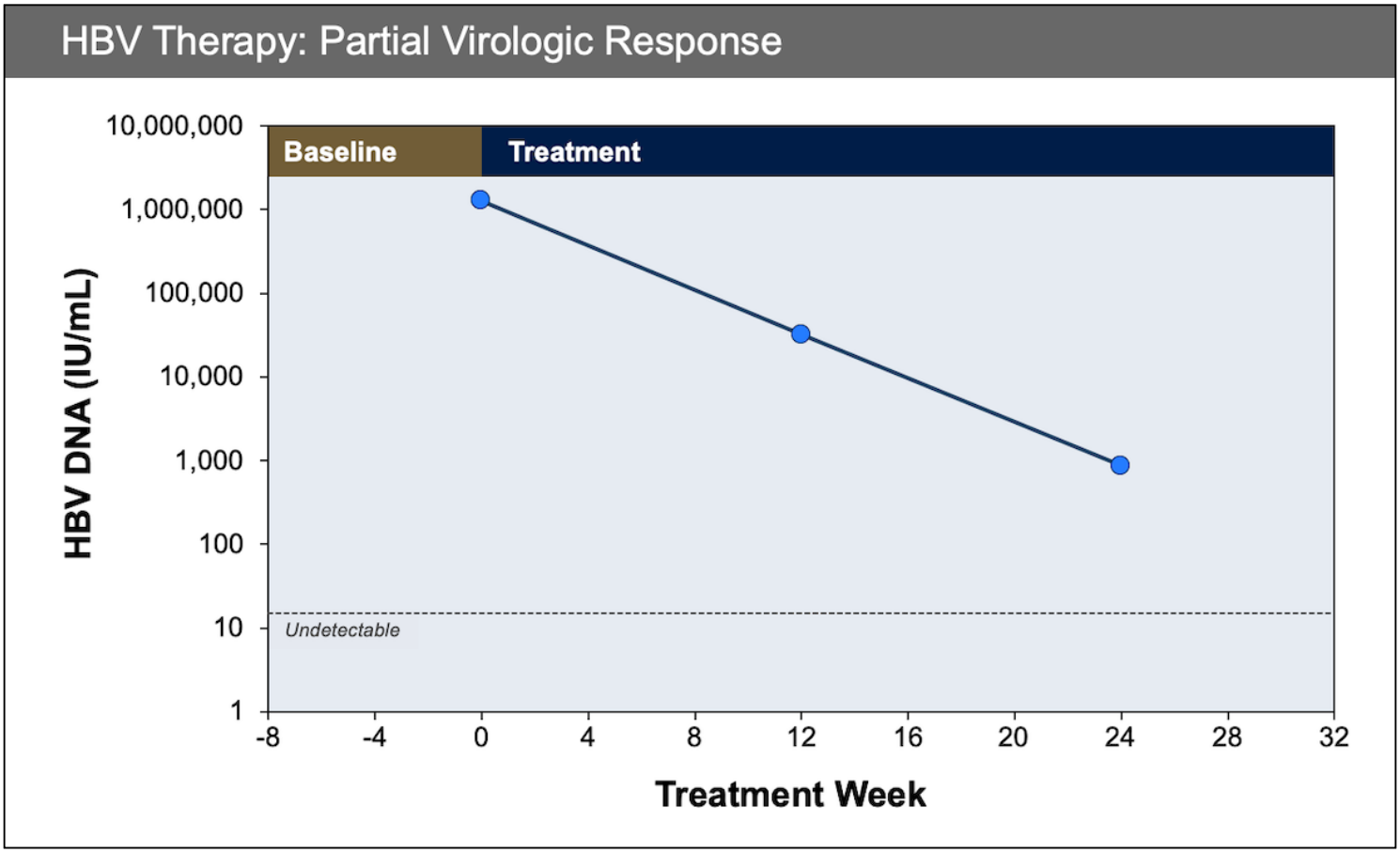

Figure 9 HBV Therapy: Complete Virologic Response

This graphic shows undetectable HBV DNA levels at 24 to 48 weeks using a real-time HBV DNA assay.

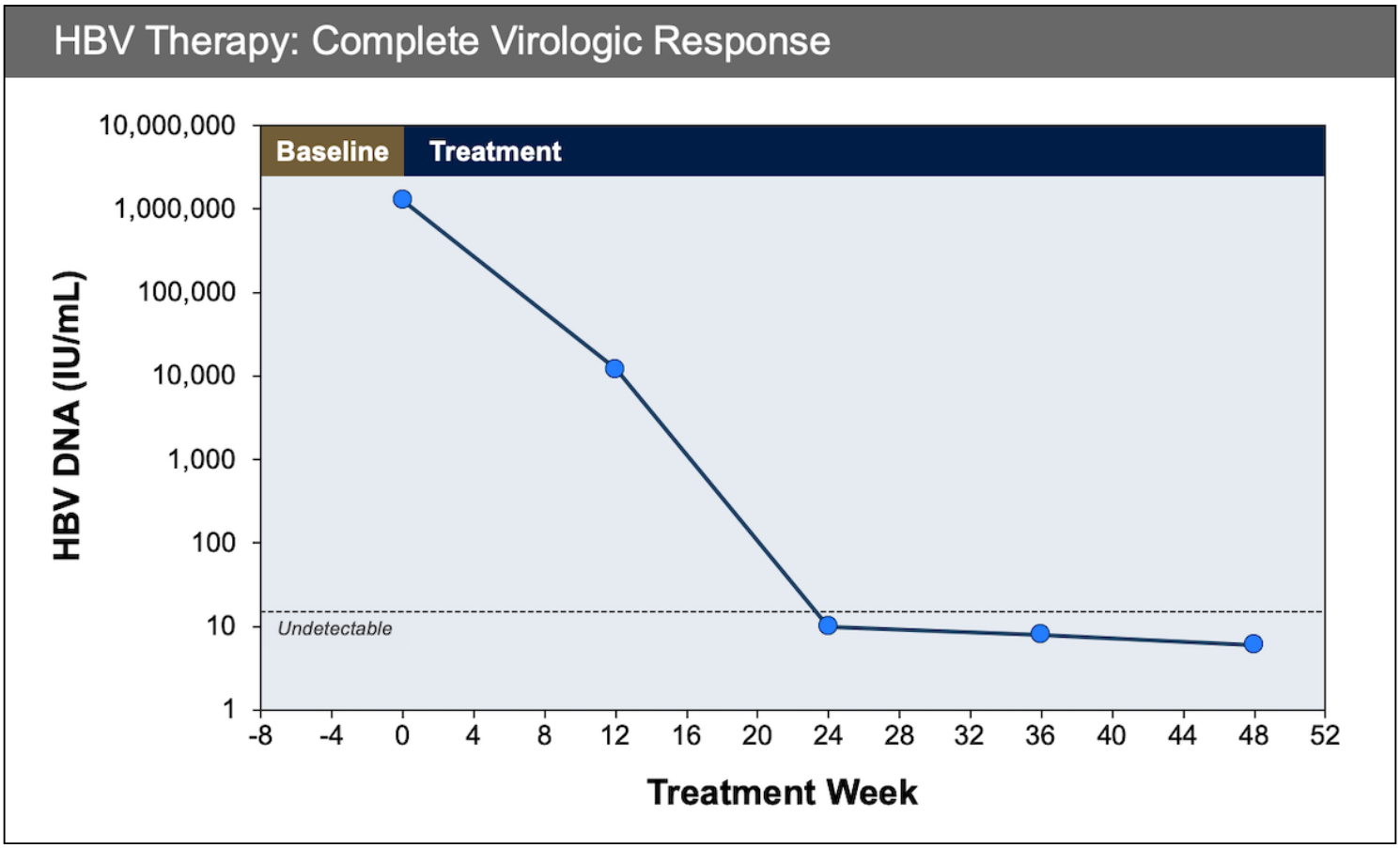

Figure 10 HBV Therapy: Maintained Virologic Response

This graphic shows a virologic response that continues while the patient is maintained on therapy for HBV.

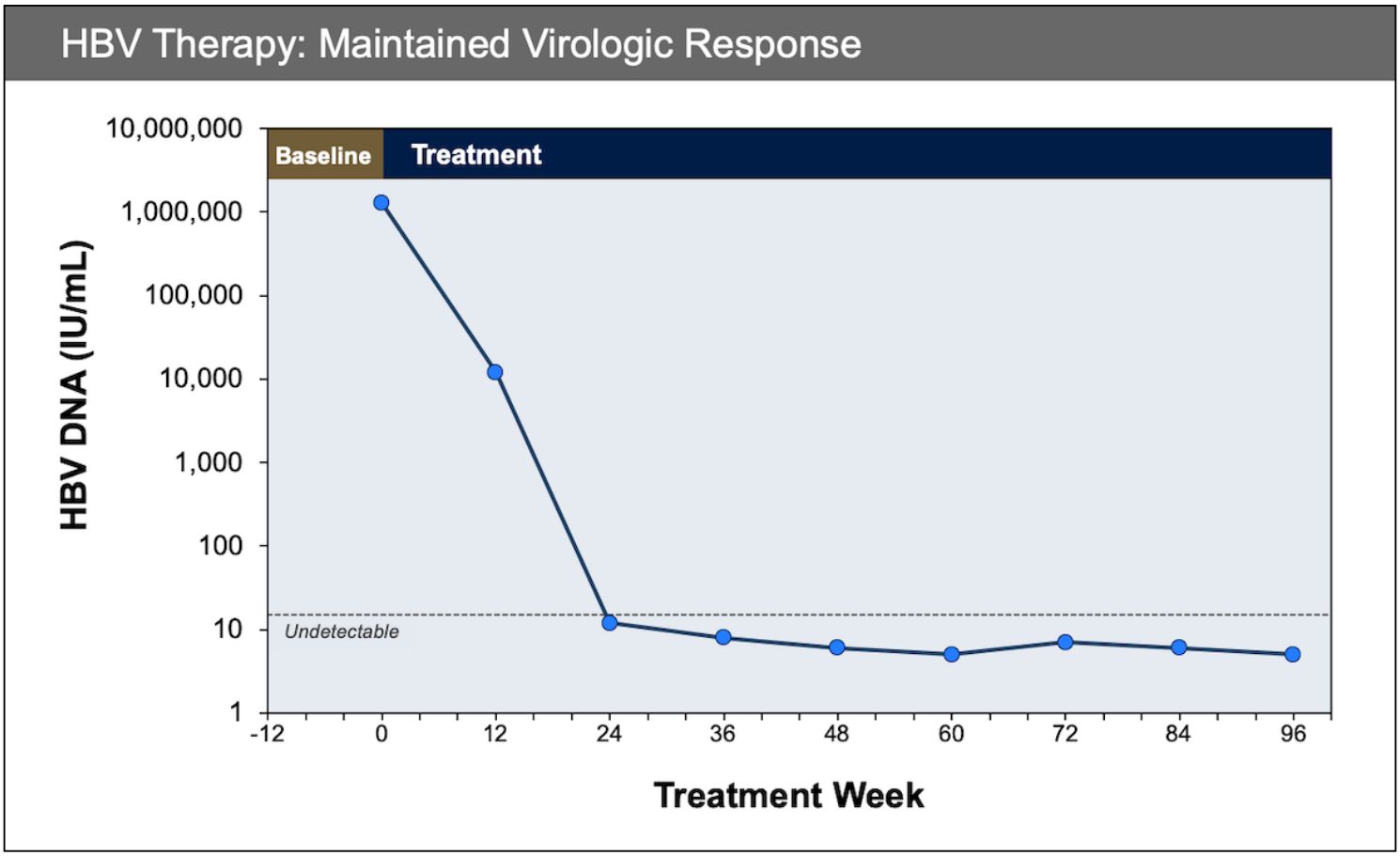

Figure 11 HBV Therapy: Sustained Virologic Response

In this example, HBV therapy is given for 120 weeks and the HBV DNA is maintained at undetectable levels for weeks 24 to 120. The HBV DNA levels remain undetectable for 48 weeks after discontinuing therapy.

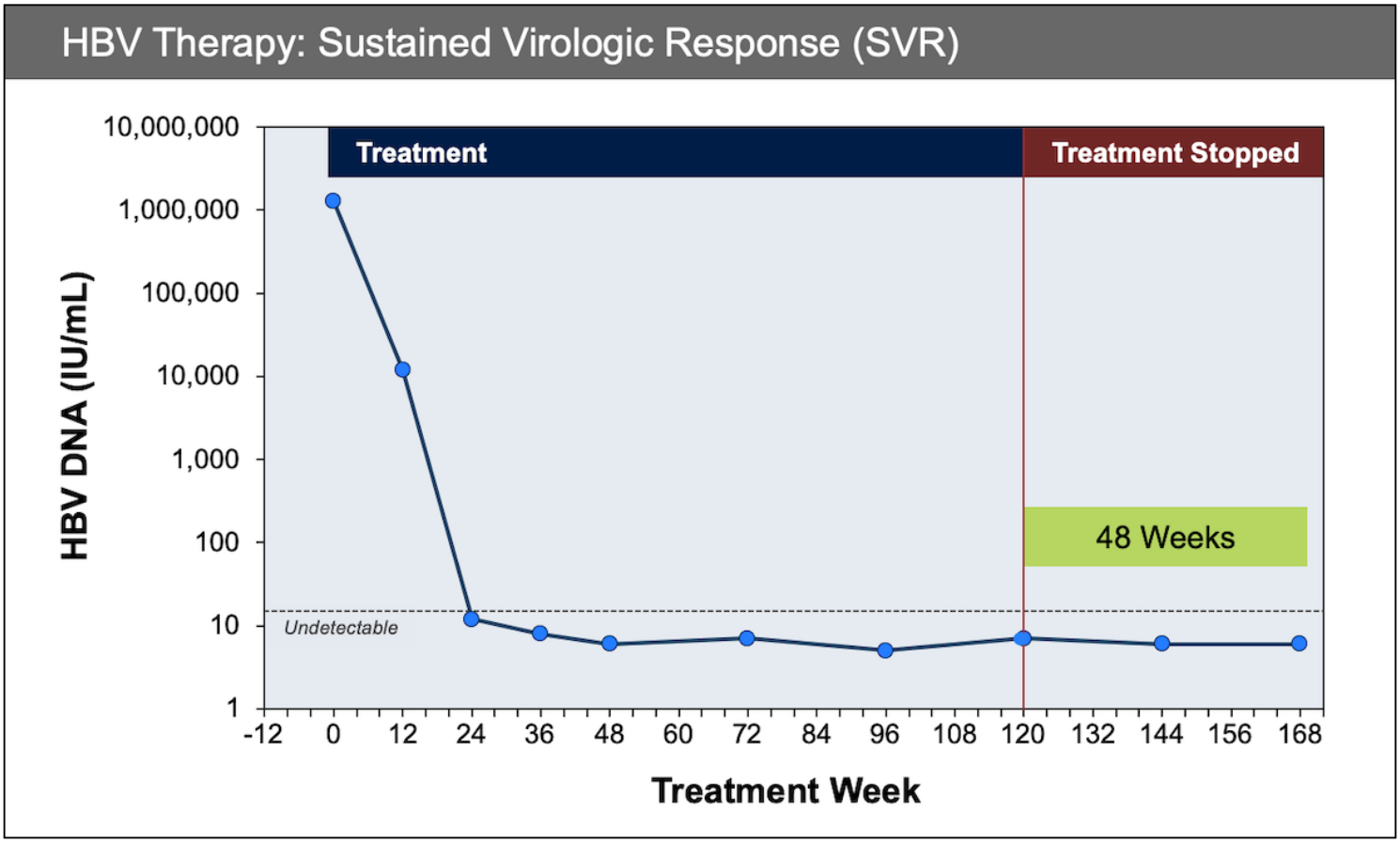

Figure 12 Definitions for Hepatitis B Virologic Responses to Treatment

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Figure 13 Liver Enzyme Elevation after Lamivudine Discontinuation in Persons with HIV-HBV Coinfection

This graph shows liver enzyme elevation after lamivudine discontinuation in persons with HIV-HBV coinfection who were enrolled in the Swiss HIV Cohort study. The graph shows the hepatotoxicity by grade severity (I-IV).

Source: Bellini C, Keiser O, Chave JP, et al. Liver enzyme elevation after lamivudine withdrawal in HIV-hepatitis B virus co-infected patients: the Swiss HIV Cohort Study. HIV Med. 2009;10:12-8.

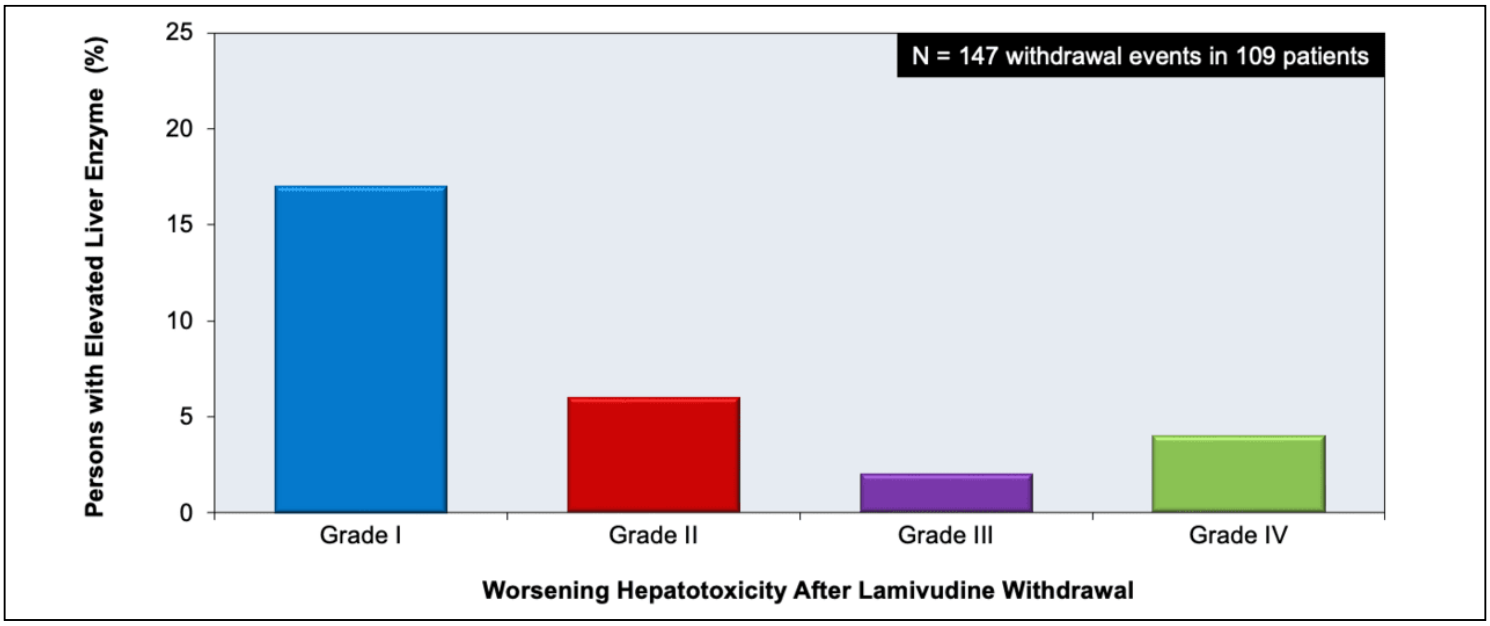

Table 1. **Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV**

Recommended Initial Regimens for People with HIV and HBV Coinfection

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use. Choice of antiretroviral therapy during pregnancy should be guided by recommendations from the Perinatal Guidelines.
For people who do NOT have a history of long-acting cabotegravir use as HIV PrEP, the following regimens are recommended:
INTI + 2 NRTIs: • Bictegravir-tenofovir alafenamide-emtricitabine (AI) • Dolutegravir plus (tenofovir alafenamide or tenofovir DF)[a] plus (emtricitabine or lamivudine) (AI)
For people with HIV and a history of using long-acting cabotegravir as HIV PrEP, integrase genotypic drug resistance testing should be done before the start of antiretroviral therapy. If treatment is begun prior to the results of genotypic testing, the following regimen is recommended:
Boosted PI + 2 NRTIs: • Darunavir (boosted with cobicistat or ritonavir) plus (tenofovir alafenamide or tenofovir DF) plus (emtricitabine or lamivudine)—pending the results of the genotype test (AIII).
Abbreviations: HBV = hepatitis B virus; INSTI = integrase strand transfer inhibitor; NRTI = nucleoside reverse transcriptase inhibitor [a]Tenofovir alafenamide and tenofovir DF are two forms of tenofovir approved by the FDA. Tenofovir alafenamide has fewer bone and kidney toxicities than tenofovir DF, whereas tenofovir DF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs. Rating of Recommendations: A = Strong; B = Moderate; C = Optional Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion

Source:

- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents HIV. Department of Health and Human Services. Considerations for antiretroviral use in patients with coinfections: hepatitis B virus/HIV coinfection. September 12, 2024. [HIV.gov]