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Hepatitis B and human immunodeficiency virus co-infection

Phung BC *et al*. Hepatitis B and HIV co-infection

Bao-Chau Phung, Philippe Sogni, Odile Launay

**Bao-Chau Phung, Philippe Sogni, Odile Launay,** Université Paris Descartes, Sorbonne Paris Cité, 75006 Paris, France

**Bao-Chau Phung, Odile Launay,** Assistance Publique-Hôpitaux de Paris AP-HP), Hôpital Cochin, CIC Cochin Pasteur, 75014 Paris, France

**Bao-Chau Phung, Odile Launay,** Inserm, CIC1417, 75014 Paris, France

**Philippe Sogni,** APHP, Service d’hépatologie, 75014 Paris, France

**Author contributions:** Phung BC wrote the paper; Launay O and Sogni P reviewed it.

**correspondence to: Odile Launay, MD, PhD, Professor,** Assistance Publique-Hôpitaux de Paris AP-HP), Hôpital Cochin, CIC Cochin Pasteur, Groupe Hospitalier Cochin - Saint, Vincent de Paul, 27 rue du Faubourg St Jacques, 75014 Paris, France. odile.launay@cch.aphp.fr

**Telephone:** +33-1-58412858 **Fax:** +33-1-58412910

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**Abstract**

Hepatitis B and human immunodeficiency virus (HBV and HIV) infection share transmission patterns and risk factors, which explains high prevalence of chronic HBV infection in HIV infected patients. The natural course of HBV disease is altered by the HIV infection with less chance to clear acute HBV infection, faster progression to cirrhosis and higher risk of liver –related death in HIV-HBV co-infected patients than in HBV mono-infected ones. HIV infected patients with chronic hepatitis B should counseled for liver damage and surveillance of chronic hepatitis B should be performed to screen early hepatocellular carcinoma. Noninvasive tools are now available to evaluate liver fibrosis. Isolated hepatitis B core antibodies (anti-HBc) are a good predictive marker of occult HBV infection. Still the prevalence and significance of occult HBV infection is controversial, but its screening may be important in the management of antiretroviral therapy. Vaccination of HBV infection is recommended in non-immune HIV patients. The optimal treatment for almost all HIV-HBV co-infected patients should contain Tenofovir plus lamivudine or emtricitabine and treatment should not be stopped to avoid HBV reactivation. Long term Tenofovir therapy may lead to significant decline in hepatitis B surface Antigen (HBs-Ag). The emergence of resistant HBV strains may compromise the HBV therapy and vaccine therapy.

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**Key words:** chronic hepatitis B; Human immunodeficiency virus; management; Occult hepatitis; Treatment

**Core tip:** Hepatitis B and human immunodeficiency virus (HBV and HIV) infection share transmission patterns and risk factors, which explains high prevalence of chronic HBV infection in HIV infected patients. The natural course of HBV disease is altered by the HIV infection with less chance to clear acute HBV infection, faster progression to cirrhosis and higher risk of liver –related death in HIV-HBV co-infected patients than in HBV mono-infected ones. The management of HBV co-infection in HIV infected persons remains a challenge. This review provides update on epidemiology, natural history, diagnosis, prevention and treatment of hepatitis B infection in HIV infected patients.

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**Introduction**

Since the advent of highly active antiretroviral treatment (HAART), human immunodeficiency virus (HIV)-associated morbidity and mortality has substantially decline. Liver diseases mainly due to hepatitis virus have emerged as a major cause of non-AIDS-related death[1,2]. As HIV and hepatitis B virus (HBV) share the same routes of transmission through sexual and percutaneous contact[3], co-infection is common. Care of hepatitis B among HIV infected individuals is a major challenge in the management of HIV infection. This review will summarize the last data on epidemiology, natural history, diagnosis, prevention and treatment of chronic hepatitis B in HIV infected patients.

**Epidemiology**

As HIV and HBV infection share common routes of transmission, the prevalence of hepatitis B markers [anti hepatitis B core antibodies (anti-HBc) and/or hepatitis B surface antigen (HBs Ag)] is very high among HIV infected persons: up to 90%[4]. Among the estimated 40 million persons infected with HIV worldwide, approximately 2-4 million (up to 10%) are chronically infected with HBV. This prevalence varies with geographic region.

In regions as Sub-Saharan Africa and east Asia, with high HBV prevalence, the majority of HBV infections occurs perinatally or during early childhood through household close contact, medical or cultural procedures like scarification or tattoo[5]; thus HBV infections are more likely to progress to chronic infections, resulting in high prevalence of chronic HBV infection among youth population at risk for sexually-acquired HIV[4]. Of note, the risk of chronicity without HBV immunization is greater (> 90%) in infants born from mothers with high viral load indirectly represented by the positivity of hepatitis B e antigen (HBe-Ag)[6]. This explains the relative low rate of vertical transmission in Africa compared with Asia due to lower prevalence of serum HBe Ag in African women with chronic hepatitis B[7].

In low HBV prevalence areas such as North America, Western Europe and Australia, HBV infection is mainly acquired in adulthood in high-risk groups, *i.e.* injection drug users (IDU) persons with multiple heterosexual partners, and men who have sex with men (MSM)[4]. Chronic HBV infection occurs in 6% to 14% of HIV-infected persons[8-10]. The highest prevalence of co-infection in western countries is among men who have sex with men (MSM)[4,10].

**Natural history**

HIV infection deleteriously affects the natural history of adult acquired HBV infection by impairing the innate and adaptive humoral and cellular immunity[6]. In immunocompromised patients, rates of chronicity after acute hepatitis B are higher, while rates of spontaneous loss of HBe Ag and/or HBs Ag and seroconversion to anti-HBe and anti-HBs are low[11–13]. Of note, acute hepatitis B resolves in 90% to 95% of immunocompetent individuals who acquire their infection in adulthood[14]. Bodsworth et al. found six fold more risks to develop chronic hepatitis B after HBV infection in HIV-infected individuals than in HIV-negative persons; the rate of HBe-Ag clearance in this study was up to five fold decreased in the HIV-infected patients[11]. It has been shown that higher CD4 cells count is correlated with higher clearance rates of HBV viremia during acute infection[6]. Nevertheless, HIV-infected persons with protective antibody to hepatitis B antigen (anti-HBs) remain at risk for loss of anti-HBs antibodies and for reactivation of HBV termed reverse seroconversion[15,16]. Hepatitis reverse seroconversion is rare (from 0.019 to 0.2 cases/100 patient-years) and occurred more frequently in the setting of HIV virologic failure[17]. Other characteristics in patients with HBV infection were reported: HIV co-infection are higher levels of HBV viremia, more frequent reactivation episodes and more rapid progression of liver fibrosis[12,18]. Several studies have also showed that HIV related immune suppression worsens the natural course of HBV infection by hastening progression to cirrhosis and liver related death[8,19]. The Swiss HIV cohort study first reported a direct effect of HIV related immunodeficiency on HBV-related hepatocellular carcinoma (HCC): 26 HCC patients were identified and matched with 251 controls and a significant association was observed between latest CD4 cell count (odd ratio per 100 cell/μl decrease= 1.33) and HCC risk[20].

As the influence of HIV infection on the course of HBV co-infection has been showed, the effects of HBV on the progression of HIV disease are controversial. In a retrospective cohort study in Greece among 1729 HIV-infected patients, no significant impact of HBV co-infection was suggested on progression to AIDS, and the meta-analysis (including 12, 382 patients from 11 studies) from the same study confirmed the absence of any effect by HBV infection on AIDS development[21]. This meta-analysis revealed increased rate of overall mortality among HIV-HBV co-infection. A higher risk for liver-related mortality in HIV-HBV co-infected individuals was found in the Multicenter Cohort Study, especially when CD4 cell nadir counts were low[8]. Data from the EuroSIDA cohort showed no impact of HBV co-infection on the occurrence of new AIDS diagnosis or AIDS defining illness but there were also increased liver-related mortality: among patients who died, mortality increased from 8% in HBs-Ag negative to 18% in HBs-Ag positive patients[10]. These findings were reinforced by data from a Thai cohort that showed no impact of hepatitis co-infection on response to combine antiretroviral therapy (cART) and on progression of HIV disease[22]. A recent study including participants from all over the world (11 countries) showed association between HBV co-infection and lower CD4 cell count at the time of HAART initiation compared with HIV mono-infected patients, especially those with high HBV DNA[23]. In a long term analysis questioning the impact of HBV on HIV outcomes while on HAART, the absence of HBV influence on HIV suppression and CD4 cell increase was found but mortality was higher in the HBV co-infected group[24].

In the French mortality survey collecting causes of death among HIV infected patients: liver related disease mostly due to hepatitis C virus (HCV) co-infection was the 3rd underlying cause of death after AIDS defining illness and cancer[25–27].

**Diagnosis of HBV infection in HIV-infected patients**

HIV-infected persons have to be tested for HBV infection. Initial testing for HBs-Ag, anti-HBs and hepatitis B core antibody (anti-HBc total) should be performed because these will identify the majority of patients with chronic hepatitis B. Some specialists would test for HBs-Ag and anti-HBs only, excluding anti-HBc, as its presence or absence does not usually affect clinical practice[28]. In practical routine, the presence of anti-HBc antibodies alone may lead to hepatitis B vaccination after occult hepatitis has been excluded (see below). Those who are diagnosed with chronic hepatitis B (presence of Hbs Ag twice during more than 6 mo) should have an initial assessment with testing for HBV DNA and hepatitis D virus (HDV) status and HCV status. Classical HBe serology testing have now little interest comparing with HBV DNA in term of risk of transmission and of treatment efficiency[29].

HBV genotyping may be part of the diagnostic tools and may be useful for predicting HBV disease progression and treatment monitoring[30]. The most prevalent HBV genotype found among HIV infected patients is type A in Europe and North America[30–32]. Association has been described between advanced liver fibrosis and genotype G[31], or between higher HBV DNA and genotypes C, D, F[23]. From the EuroSIDA cohort, higher HBV DNA levels have been associated with HBV genotype A[33]. However, HBV genotyping is not well defined in the scheme of HBV management and is not performed in practical routine.

Until now the need for HBV drug resistance testing prior to starting HBV treatment has not been demonstrated[23]. HBV resistance testing should be performed in case of detectable HBV viremia in patients who have already received lamivudine. Nevertheless, no impact of lamivudine resistance has been showed on long-term efficacy of tenofovir[34].

Occult HBV infection is defined by the presence of HBV in plasma and/or in liver tissue of patients without detectable HBs-Ag. Conflicting results have been reported on its prevalence ranging from very low (less than 0.1%) to higher prevalence, 35% reported in a French cohort[35]. An early study reported up to 90% prevalence of occult hepatitis B[36], while most studies found prevalence around 10% to 20 %[37–40]. This wide range may be explained by the heterogeneity of study populations and the usage of different sensitivity and specificity of HBV DNA assays[39,41]. Isolated anti-HBc is good predictive marker of occult HBV, and HBV DNA should be tested in the pattern of anti-HBc alone when patients exhibit serum transaminases abnormalities or liver failure[42]. Still the contribution of occult HBV on liver damage remains unclear[43]. But screening of occult HBV infection may have implications in terms of antiretroviral therapy and risk of immune reconstitution[42].

Liver fibrosis has to be assessed because it will establish a prognostic value and will be part of the therapeutic decisions. Noninvasive tools such as transient elastography (FibroScan) or serum biochemical indexes (Fibrotest) are now available to evaluate liver fibrosis[44–46]; though these tools are not accurate do discriminate intermediate stages of fibrosis[47], the combined use of fibroscan and fibrotest can improve the diagnostic accuracy and reduce the need for liver biopsy which stays the current gold standard[48,49].

**Hepatitis B prevention**

Current guidelines recommend that HIV-infected patients who have no serological markers against HBV (HBs Ag, anti HBs and anti-HBc negative) should be offered vaccination with a dosage of anti-Hbs antibodies 1 to 2 mo after the end of the complete scheme[28,50,51]. The standard vaccine schedule (3 doses at 0, 1 and 6 mo) is impaired in HIV-infected subjects compared to healthy persons[52]. A four double doses of hepatitis B vaccine regimen (40 ug given at 0, 1, 2 and 6 mo) has showed improved serological response (*i.e* anti-HBs antibodies above 10 UI/ml) in HIV infected subjects[53] and has been recently recommended in French guidelines. This scheme is also of interest regarding the high rate of patients achieving anti-HBs titers above 100 IU/l (Table 1)

In the absence of seroprotection (anti-HBs antibodies < 10 IU/l) at the end of vaccination, one to three additional doses of HBV vaccine should be administered. For patients with seroconversion, anti-HBs levels should rechecked every year in order to administer booster vaccine dose when anti-HBs levels decline < 10 IU/l.

The management of patients with isolated anti-HBc is not clear. This serological pattern might reflect exposure in the past following which anti-HBs antibodies did not develop or have fallen below the detection level[54] or more rarely occult HBV infection[42]. The CDC guidelines recommend to administer one dose of hepatitis B vaccine and determine the serological response 2-4 wk later[28]. If an adequate protective antibody level is revealed, immunization is complete. If not, HBV DNA should be tested to assess occult HBV infection[29]. If no HBV DNA is detected, some recommend a complete scheme of HBV vaccination[55].

In case of failure of repeat immunization, serological markers of HBV should be monitored annually, and including tenofovir in the cART can be considered.

**Management of chronic hepatitis B in HIV infected patients**

HIV-infected subjects should be counseled regarding prevention of liver damage: limitation of alcohol consumption[56], avoiding hepatotoxic drugs (common use of paracetamol). They also should be vaccinated against hepatitis A virus (HAV) if not immune: HAV superinfection has been associated with high risk of liver failure and death in patients with underlying chronic liver disease[57,58].

Surveillance of chronic hepatitis B infection using abdominal ultrasound every 6 mo should be performed to detect early HCC in patients at risk: that is to say cirrhotic patients, but also non-cirrhotic HBV carriers with active hepatitis or family history of HCC, and non-cirrhotic patients with chronic hepatitis C and advanced liver fibrosis F3[59]. Serum alpha-fetoprotein (AFP) has a suboptimal performance but can be associated in the surveillance of chronic hepatitis B[59].

Cirrhotic patients should be monitored for the presence of esophageal varices using upper-gastrointestinal endoscopy every 1-2 year.

**Treatment of chronic hepatitis B in HIV infected patients**

The indication of chronic hepatitis B treatment in HIV infected individuals is based on a list of several considerations: the indication of cART for HIV infection, the stage of the liver disease and its risk to progression to clinically significant liver complications[60]. The goal of HBV treatment is in the best case to achieve HBs Ag clearance with anti-HBs seroconversion, but this objective is rarely reached (less than 10% of HBV mono-infected patients under interferon treatment and probably even less in HIV-HBV co-infected patients)[29]. In practical routines the objectives for HBV treatment are: normalization of alanine aminotransferase (ALT), HBe-Ag seroconversion as HBe-Ag loss was associated with better histological liver evolution[61], and mainly sustained suppression of HBV replication to reduce liver inflammation and to stop or delay progression of fibrosis, to avoid development of cirrhosis, decompensation, HCC and liver related death[29].

Drugs that have been approved in Europe for the treatment of HBV include standard interferon (INF) replaced by pegylated interferon (pegINF), lamivudine (3TC), adefovir (ADV), entecavir (ETV) and telbivudine (LdT). Tenofovir (TDF) and emtricitabine (FTC) are approved for HIV and are also active against HBV. It is essential in the management of HBV treatment to avoid the development of HBV associated drug resistance, which has already emerged under lamivudine monotherapy (occurring in more than 80% of patients after 5 years of treatment)[51]. Furthermore a subset of lamivudine–resistant HBV isolates may behave as vaccine escapes mutants. The incidence of mutants selected by nucleos(t)ide analogues (NA) seem to be increasing and thus problematic especially in limited resources settings where there is restrained access to powerful anti-HBV drugs[62]. ETV Monotherapy showed low rates (1.2%) of resistance in nucleosive-naïve patients treated for up to 5 years, but this rate increases to 51% in patients with lamivudine resistance[63]. TDF offers the benefit of no evidence of developing TDF-resistance mutations after monitoring up to 7 years, with no effect of 3TC prior exposure and/or resistance[64,65].

When HIV infection does not require treatment, which should be a less frequent situation as European and United States guidelines, recommend early HIV treatment initiation, algorithm for HBV treatment is based on serum HBV DNA, ALT and liver fibrosis staging. Treatment is advised when viremia is above 2000 IU/ml or ALT are elevated, or both, but also when advanced liver fibrosis is seen (with or without HBV DNA/ALT abnormalities)[60]. Treatment options for HBV infection should include agents without HIV antiviral activity to reduce risk of viral resistance[60]. PegINF based therapy for a finite course of 12 mo is an option with possible benefit of sustained response in particular when HBe-Ag positive, elevated ALT and low serum HBV DNA. But the rate of such response is low[66], and the frequent side effects with bad impact on the quality of life of pegINF limit its use[67,68]. Monotherapy of adefovir is an alternative but given the risk of selecting drug resistance, an early “add-on” strategy should be considered when criteria of undetectable HBV viremia is not met at week 24 of therapy[69].

When both HIV and HBV infections meet criteria to be treated, which will turn to be the most frequent situation regarding recent guidelines for HIV treatment, the combination of TDF and FTC (or lamivudine) is the preferred choice[50,70]. In case of prior exposure to lamivudine with selected resistance to lamivudine, TDF is recommended because it has demonstrated its activity toward lamivudine-resistant HBV[71]. A recent meta-analysis confirmed the durable suppression of HBV viremia with no impact of previous lamivudine exposure[64]. Combine therapy is recommended but until now no significant benefit of combine therapy over TDF alone has been demonstrated[32,64].

Seroclearance of HBs-Ag is a rare outcome during long term HBV therapy with potent nucleos(t)ide analogues. Dutch study investigated long term HBs Ag level kinetics in HIV-HBV co-infected patients treated with tenofovir[72], and showed that the decline in HBs-Ag was essentially found among HBe Ag positive HIV-HBV co-infected patients. It also showed that long term TDF therapy leads to significant decline in HBs-Ag, that there was a correlation between CD4 cells count and HBs Ag level kinetics and that HBs Ag kinetics early during treatment were predictive of HBs-Ag seroclearance[72].

Hepatitis delta virus (HDV) has a unique replication progress that requires co-infection with HBV. It suppresses HBV replication but it causes severe liver disease with rapid progression to cirrhosis (10%-15% of patients within 2 years)[73,74]. The prevalence of anti-HDV in HBV-HIV co-infected patients in EuroSIDA cohort is 14.5%[75]. Delta hepatitis increases the risk of liver related death and overall mortality in HIV infected patients[75]. Interferon therapy is the only evidence-based treatment for HDV, still a small study has pointed out the potential benefit of potent anti-HBV NA therapy in chronic delta hepatitis[76].

Patients under treatment should be monitored to assess response. A durable anti-HBe seroconversion in HBe-Ag positive patients is a marker of clinical relevant response. When using nucleot(s)ide analogues initial response is defined as at least 1 log10 drop in HBV DNA levels within 3 mo. HBV DNA should then be measured every 3 mo.

Treatment efficacy is measured by the HBV DNA negativation below the lower limit of detection, ideally after 6-12 mo of treatment[28].

Resistance should be suspected in compliant patients if HBV DNA levels increase by 1 log10 or more, if available resistance testing should be performed[29]. Non or poor adherence to treatment remains the first diagnostic in case of failure[77,78].

Discontinuation of anti-HBV treatment can result in potentially fatal hepatitis flares[79] and should be avoid when possible.

Add-on pegINF in HBe-Ag HIV co-infected patients under treatment with TDF and undetectable HBV DNA did not seem to increase rates of HBe-Ag seroconversion[80].

**Conclusion**

What should not be forgotten is that HBV persists in the liver even after successful immunological control of the infection, therefore HBV infected patients are at risk of HBV reactivation. As HIV infection worsens the course of HBV infection with more severe outcome of the liver disease and higher rates of mortality, HBV status should be assessed in HIV-infected patients. Patients with negative HBs Ag and negative anti-HBs and anti-HBc antibodies should be offered vaccination and HBV co-infected patients should be treated regardless of the CD4 count. Tenofovir plus lamivudine or emtricitabine with a third agent should the recommended first line therapy for almost all HIV-infected HBs Ag patients. HBV treatment should not be stopped because long-term therapy can possibly lead to HBs Ag loss and because of the risk HBV reactivation. Besides, the initiation of cART can also lead to an immune restoration disease with immune mediated injury. Periodic liver fibrosis assessment is warranted in HBV-HIV co-infected patients using non-invasive tools. Some challenges remain as optimizing the assessment of HBV infection in the context of HIV, the emergence and spreading of resistant HBV strains compromising HBV therapy and vaccine strategy (vaccine escape mutants).

**REFERENCES**

1 **Weber R**, Sabin CA, Friis-Møller N, Reiss P, El-Sadr WM, Kirk O, Dabis F, Law MG, Pradier C, De Wit S, Akerlund B, Calvo G, Monforte Ad, Rickenbach M, Ledergerber B, Phillips AN, Lundgren JD. Liver-related deaths in persons infected with the human immunodeficiency virus: the D: A: D study. *Arch Intern Med* 2006; **166**: 1632-1641 [PMID: 16908797]

2 **Salmon-Ceron D**, Lewden C, Morlat P, Bévilacqua S, Jougla E, Bonnet F, Héripret L, Costagliola D, May T, Chêne G; Mortality 2000 study group. Liver disease as a major cause of death among HIV infected patients: role of hepatitis C and B viruses and alcohol. *J Hepatol* 2005; **42**: 799-805 [PMID: 15973779]

3 **Shire NJ**, Sherman KE. Management of HBV/HIV-coinfected Patients. *Semin Liver Dis* 2005; **25** Suppl 1: 48-57 [PMID: 16103981 DOI: 10.1055/s-2005-915646]

4 **Alter MJ**. Epidemiology of viral hepatitis and HIV co-infection. *J Hepatol* 2006; **44**: S6-S9 [PMID: 16352363]

5 **Modi AA**, Feld JJ. Viral hepatitis and HIV in Africa. *AIDS Rev* 2007; **9**: 25-39 [PMID: 17474311]

6 **McGovern BH**. The epidemiology, natural history and prevention of hepatitis B: implications of HIV coinfection. *Antivir Ther* 2007; **12** Suppl 3: H3-13 [PMID: 18284178]

7 **Hoffmann CJ**, Thio CL. Clinical implications of HIV and hepatitis B co-infection in Asia and Africa. *Lancet Infect Dis* 2007; **7**: 402-409 [PMID: 17521593 DOI: 10.1016/S1473-3099(07)70135-4]

8 **Thio CL**, Seaberg EC, Skolasky R, Phair J, Visscher B, Muñoz A, Thomas DL; Multicenter AIDS Cohort Study. HIV-1, hepatitis B virus, and risk of liver-related mortality in the Multicenter Cohort Study (MACS). *Lancet* 2002; **360**: 1921-1926 [PMID: 12493258 DOI: 10.1016/S0140-6736(02)11913-1]

9 **Kellerman SE**, Hanson DL, McNaghten AD, Fleming PL. Prevalence of chronic hepatitis B and incidence of acute hepatitis B infection in human immunodeficiency virus-infected subjects. *J Infect Dis* 2003; **188**: 571-577 [PMID: 12898445 DOI: 10.1086/377135]

10 **Konopnicki D**, Mocroft A, de Wit S, Antunes F, Ledergerber B, Katlama C, Zilmer K, Vella S, Kirk O, Lundgren JD. Hepatitis B and HIV: prevalence, AIDS progression, response to highly active antiretroviral therapy and increased mortality in the EuroSIDA cohort. *AIDS* 2005; **19**: 593-601 [PMID: 15802978 DOI: 10.1097/01.aids.0000163936.99401.fe]

11 **Bodsworth NJ**, Cooper DA, Donovan B. The influence of human immunodeficiency virus type 1 infection on the development of the hepatitis B virus carrier state. *J Infect Dis* 1991; **163**: 1138-1140 [PMID: 2019762 DOI: 10.1093/infdis/163.5.1138]

12 **Puoti M**, Torti C, Bruno R, Filice G, Carosi G. Natural history of chronic hepatitis B in co-infected patients. *J Hepatol* 2006; **44**: S65-S70 [PMID: 16338021]

13 **Thio CL**. Hepatitis B and human immunodeficiency virus coinfection. *Hepatology* 2009; **49**: S138-S145 [PMID: 19399813]

14 **Thimme R**, Spangenberg HC, Blum HE. Hepatitis B or hepatitis C and human immunodeficiency virus infection. *J Hepatol* 2005; **42** Suppl: S37-S44 [PMID: 15777571]

15 **Biggar RJ**, Goedert JJ, Hoofnagle J. Accelerated loss of antibody to hepatitis B surface antigen among immunodeficient homosexual men infected with HIV. *N Engl J Med* 1987; **316**: 630-631 [PMID: 3807959 DOI: 10.1056/NEJM198703053161015]

16 **Laukamm-Josten U**, Müller O, Bienzle U, Feldmeier H, Uy A, Guggenmoos-Holzmann I. Decline of naturally acquired antibodies to hepatitis B surface antigen in HIV-1 infected homosexual men. *AIDS* 1988; **2**: 400-401 [PMID: 3146272 DOI: 10.1097/00002030-198810000-00014]

17 **Rouphael NG**, Talati NJ, Rimland D. Hepatitis B reverse seroconversion in HIV-positive patients: case series and review of the literature. *AIDS* 2007; **21**: 771-774 [PMID: 17413702 DOI: 10.1097/QAD.0b013e3280ad47f5]

18 **Gilson RJ**, Hawkins AE, Beecham MR, Ross E, Waite J, Briggs M, McNally T, Kelly GE, Tedder RS, Weller IV. Interactions between HIV and hepatitis B virus in homosexual men: effects on the natural history of infection. *AIDS* 1997; **11**: 597-606 [PMID: 9108941 DOI: 10.1097/00002030-199705000-00007]

19 **Colin JF**, Cazals-Hatem D, Loriot MA, Martinot-Peignoux M, Pham BN, Auperin A, Degott C, Benhamou JP, Erlinger S, Valla D, Marcellin P. Influence of human immunodeficiency virus infection on chronic hepatitis B in homosexual men. *Hepatology* 1999; **29**: 1306-1310 [PMID: 10094979]

20 **Clifford GM**, Rickenbach M, Polesel J, Dal Maso L, Steffen I, Ledergerber B, Rauch A, Probst-Hensch NM, Bouchardy C, Levi F, Franceschi S. Influence of HIV-related immunodeficiency on the risk of hepatocellular carcinoma. *AIDS* 2008; **22**: 2135-2141 [PMID: 18832877]

21 **Nikolopoulos GK**, Paraskevis D, Hatzitheodorou E, Moschidis Z, Sypsa V, Zavitsanos X, Kalapothaki V, Hatzakis A. Impact of hepatitis B virus infection on the progression of AIDS and mortality in HIV-infected individuals: a cohort study and meta-analysis. *Clin Infect Dis* 2009; **48**: 1763-1771 [PMID: 19435436 DOI: 10.1086/599110]

22 **Law WP**, Duncombe CJ, Mahanontharit A, Boyd MA, Ruxrungtham K, Lange JM, Phanuphak P, Cooper DA, Dore GJ. Impact of viral hepatitis co-infection on response to antiretroviral therapy and HIV disease progression in the HIV-NAT cohort. *AIDS* 2004; **18**: 1169-1177 [PMID: 15166532 DOI: 10.1097/00002030-200405210-00010]

23 **Thio CL**, Smeaton L, Saulynas M, Hwang H, Saravanan S, Kulkarni S, Hakim J, Nyirenda M, Iqbal HS, Lalloo UG, Mehta AS, Hollabaugh K, Campbell TB, Lockman S, Currier JS. Characterization of HIV-HBV coinfection in a multinational HIV-infected cohort. *AIDS* 2013; **27**: 191-201 [PMID: 23032418]

24 **Hoffmann CJ**, Seaberg EC, Young S, Witt MD, D'Acunto K, Phair J, Thio CL. Hepatitis B and long-term HIV outcomes in coinfected HAART recipients. *AIDS* 2009; **23**: 1881-1889 [PMID: 19550291 DOI: 10.1097/QAD.0b013e32832e463a]

25 **Lewden C**, Salmon D, Morlat P, Bévilacqua S, Jougla E, Bonnet F, Héripret L, Costagliola D, May T, Chêne G. Causes of death among human immunodeficiency virus (HIV)-infected adults in the era of potent antiretroviral therapy: emerging role of hepatitis and cancers, persistent role of AIDS. *Int J Epidemiol* 2005; **34**: 121-130 [PMID: 15561752]

26 **Lewden C**, May T, Rosenthal E, Burty C, Bonnet F, Costagliola D, Jougla E, Semaille C, Morlat P, Salmon D, Cacoub P, Chêne G. Changes in causes of death among adults infected by HIV between 2000 and 2005: The "Mortalité 2000 and 2005" surveys (ANRS EN19 and Mortavic). *J Acquir Immune Defic Syndr* 2008; **48**: 590-598 [PMID: 18645512]

27 **Roussillon C**, Henard S, Hardel L, Rosenthal E, Aouba A, Bonnet F, Couturier F, Cacoub P, May T, Salmon D, Chene G, Morlat P. Groupe Mortalité 2010, Causes de décès des patients infectés par le VIH en France en 2010. Étude ANRS EN20 Mortalité 2010. Numéro thématique. VIH/sida en France : données de surveillance et études. 2012

28 **Kaplan JE**, Benson C, Holmes KK, Brooks JT, Pau A, Masur H; Centers for Disease Control and Prevention (CDC); National Institutes of Health; HIV Medicine Association of the Infectious Diseases Society of America. Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. *MMWR Recomm Rep* 2009; **58**: 1-207; quiz CE1-4 [PMID: 19357635]

29 **Alberti A**, Clumeck N, Collins S, Gerlich W, Lundgren J, Palù G, Reiss P, Thiebaut R, Weiland O, Yazdanpanah Y, Zeuzem S. Short statement of the first European Consensus Conference on the treatment of chronic hepatitis B and C in HIV co-infected patients. *J Hepatol* 2005; **42**: 615-624 [PMID: 15916745 DOI: 10.1016/j.jhep.2005.03.003]

30 **Soriano V**, Sheldon J, Ramos B, Núñez M. Confronting chronic hepatitis B virus infection in HIV: new diagnostic tools and more weapons. *AIDS* 2006; **20**: 451-453 [PMID: 16439880 DOI: 10.1097/01.aids.0000200538.25103.3a]

31 **Lacombe K**, Massari V, Girard PM, Serfaty L, Gozlan J, Pialoux G, Mialhes P, Molina JM, Lascoux-Combe C, Wendum D, Carrat F, Zoulim F. Major role of hepatitis B genotypes in liver fibrosis during coinfection with HIV. *AIDS* 2006; **20**: 419-427 [PMID: 16439876]

32 **Piroth L**, Pol S, Lacombe K, Miailhes P, Rami A, Rey D, Loustau-Ratti V, Morlat P, Goderel I, Sene D, Rosenthal E, Carrat F, Cacoub P. Management and treatment of chronic hepatitis B virus infection in HIV positive and negative patients: the EPIB 2008 study. *J Hepatol* 2010; **53**: 1006-1012 [PMID: 20800920]

33 **Soriano V**, Mocroft A, Peters L, Rockstroh J, Antunes F, Kirkby N, de Wit S, Monforte Ad, Flisiak R, Lundgren J. Predictors of hepatitis B virus genotype and viraemia in HIV-infected patients with chronic hepatitis B in Europe. *J Antimicrob Chemother* 2010; **65**: 548-555 [PMID: 20051475 DOI: 10.1093/jac/dkp479]

34 **de Vries-Sluijs TE**, Reijnders JG, Hansen BE, Zaaijer HL, Prins JM, Pas SD, Schutten M, Hoepelman AI, Richter C, Mulder JW, de Man RA, Janssen HL, van der Ende ME. Long-term therapy with tenofovir is effective for patients co-infected with human immunodeficiency virus and hepatitis B virus. *Gastroenterology* 2010; **139**: 1934-1941 [PMID: 20801123]

35 **Piroth L**, Lafon ME, Binquet C, Bertillon P, Gervais A, Lootvoet E, Lang JM, De Jaureguiberry JP, Chene G, Leport C. Occult hepatitis B in HIV-HCV coinfected patients. *Scand J Infect Dis* 2008; **40**: 835-839 [PMID: 18609222]

36 **Hofer M**, Joller-Jemelka HI, Grob PJ, Lüthy R, Opravil M. Frequent chronic hepatitis B virus infection in HIV-infected patients positive for antibody to hepatitis B core antigen only. Swiss HIV Cohort Study. *Eur J Clin Microbiol Infect Dis* 1998; **17**: 6-13 [PMID: 9512175 DOI: 10.1007/BF01584356]

37 **Cohen Stuart JW**, Velema M, Schuurman R, Boucher CA, Hoepelman AI. Occult hepatitis B in persons infected with HIV is associated with low CD4 counts and resolves during antiretroviral therapy. *J Med Virol* 2009; **81**: 441-445 [PMID: 19152397 DOI: 10.1002/jmv.21422]

38 **Morsica G**, Ancarani F, Bagaglio S, Maracci M, Cicconi P, Cozzi Lepri A, Antonucci G, Bruno R, Santantonio T, Tacconi L, Baldelli F, Piscopo R, Santoro D, Lazzarin A, D'Arminio Monforte A. Occult hepatitis B virus infection in a cohort of HIV-positive patients: correlation with hepatitis C virus coinfection, virological and immunological features. *Infection* 2009; **37**: 445-449 [PMID: 19669092 DOI: 10.1007/s15010-008-8194-9]

39 **Khamduang W**, Ngo-Giang-Huong N, Gaudy-Graffin C, Jourdain G, Suwankornsakul W, Jarupanich T, Chalermpolprapa V, Nanta S, Puarattana-Aroonkorn N, Tonmat S, Lallemant M, Goudeau A, Sirirungsi W. Prevalence, risk factors, and impact of isolated antibody to hepatitis B core antigen and occult hepatitis B virus infection in HIV-1-infected pregnant women. *Clin Infect Dis* 2013; **56**: 1704-1712 [PMID: 23487379 DOI: 10.1093/cid/cit166]

40 **Shire NJ**, Rouster SD, Stanford SD, Blackard JT, Martin CM, Fichtenbaum CJ, Sherman KE. The prevalence and significance of occult hepatitis B virus in a prospective cohort of HIV-infected patients. *J Acquir Immune Defic Syndr* 2007; **44**: 309-314 [PMID: 17159656 DOI: 10.1097/QAI.0b013e31802e29a9]

41 **Sun HY**, Lee HC, Liu CE, Yang CL, Su SC, Ko WC, Lin CY, Tsai JJ, Wong WW, Ho MW, Cheng SH, Lin YH, Miao WJ, Hung CC. Factors associated with isolated anti-hepatitis B core antibody in HIV-positive patients: impact of compromised immunity. *J Viral Hepat* 2010; **17**: 578-587 [PMID: 19818002]

42 **Shire NJ**, Rouster SD, Rajicic N, Sherman KE. Occult hepatitis B in HIV-infected patients. *J Acquir Immune Defic Syndr* 2004; **36**: 869-875 [PMID: 15213572 DOI: 10.1097/00126334-200407010-00015]

43 **Tramuto F**, Maida CM, Colomba GM, Di Carlo P, Vitale F. Prevalence of occult hepatitis B virus infection in a cohort of HIV-positive patients resident in Sicily, Italy. *Biomed Res Int* 2013; **2013**: 859583 [PMID: 24063015]

44 **Marcellin P**, Ziol M, Bedossa P, Douvin C, Poupon R, de Lédinghen V, Beaugrand M. Non-invasive assessment of liver fibrosis by stiffness measurement in patients with chronic hepatitis B. *Liver Int* 2009; **29**: 242-247 [PMID: 18637064 DOI: 10.1111/j.1478-3231.2008.01802.x]

45 **Ziol M**, Handra-Luca A, Kettaneh A, Christidis C, Mal F, Kazemi F, de Lédinghen V, Marcellin P, Dhumeaux D, Trinchet JC, Beaugrand M. Noninvasive assessment of liver fibrosis by measurement of stiffness in patients with chronic hepatitis C. *Hepatology* 2005; **41**: 48-54 [PMID: 15690481]

46 **Myers RP**, Tainturier MH, Ratziu V, Piton A, Thibault V, Imbert-Bismut F, Messous D, Charlotte F, Di Martino V, Benhamou Y, Poynard T. Prediction of liver histological lesions with biochemical markers in patients with chronic hepatitis B. *J Hepatol* 2003; **39**: 222-230 [PMID: 12873819 DOI: 10.1016/S0168-8278(03)00171-5]

47 **Moreno S**, García-Samaniego J, Moreno A, Ortega E, Pineda JA, del Romero J, Tural C, von Wichmann MA, Berenguer J, Castro A, Espacio R. Noninvasive diagnosis of liver fibrosis in patients with HIV infection and HCV/HBV co-infection. *J Viral Hepat* 2009; **16**: 249-258 [PMID: 19215579 DOI: 10.1111/j.1365-2893.2009.01088.x]

48 **Castéra L**, Vergniol J, Foucher J, Le Bail B, Chanteloup E, Haaser M, Darriet M, Couzigou P, De Lédinghen V. Prospective comparison of transient elastography, Fibrotest, APRI, and liver biopsy for the assessment of fibrosis in chronic hepatitis C. *Gastroenterology* 2005; **128**: 343-350 [PMID: 15685546 DOI: 10.1053/j.gastro.2004.11.018]

49 **Castera L**. Hepatitis B: are non-invasive markers of liver fibrosis reliable? *Liver Int* 2014; **34** Suppl 1: 91-96 [PMID: 24373084 DOI: 10.1111/liv.12393]

50 **Brook G**, Main J, Nelson M, Bhagani S, Wilkins E, Leen C, Fisher M, Gilleece Y, Gilson R, Freedman A, Kulasegaram R, Agarwal K, Sabin C, Deacon-Adams C. British HIV Association guidelines for the management of coinfection with HIV-1 and hepatitis B or C virus 2010. *HIV Med* 2010; **11**: 1-30 [PMID: 20059574 DOI: 10.1111/j.1468-1293.2009.00781.x]

51 **Rockstroh JK**, Bhagani S, Benhamou Y, Bruno R, Mauss S, Peters L, Puoti M, Soriano V, Tural C. European AIDS Clinical Society (EACS) guidelines for the clinical management and treatment of chronic hepatitis B and C coinfection in HIV-infected adults. *HIV Med* 2008; **9**: 82-88 [PMID: 18257771 DOI: 10.1111/j.1468-1293.2007.00535.x]

52 **Mehta N**, Cunningham CK, Flynn P, Pepe J, Obaro S, Kapogiannis BG, Bethel J, Luzuriaga K. Impaired generation of hepatitis B virus-specific memory B cells in HIV infected individuals following vaccination. *Vaccine* 2010; **28**: 3672-3678 [PMID: 20356567 DOI: 10.1016/j.vaccine.2010.03.022]

53 **Launay O**, van der Vliet D, Rosenberg AR, Michel ML, Piroth L, Rey D, Colin de Verdière N, Slama L, Martin K, Lortholary O, Carrat F. Safety and immunogenicity of 4 intramuscular double doses and 4 intradermal low doses vs standard hepatitis B vaccine regimen in adults with HIV-1: a randomized controlled trial. *JAMA* 2011; **305**: 1432-1440 [PMID: 21486976 DOI: 10.1001/jama.2011.351]

54 **Grob P**, Jilg W, Bornhak H, Gerken G, Gerlich W, Günther S, Hess G, Hüdig H, Kitchen A, Margolis H, Michel G, Trepo C, Will H, Zanetti A, Mushahwar I. Serological pattern "anti-HBc alone": report on a workshop. *J Med Virol* 2000; **62**: 450-455 [PMID: 11074473 DOI: 10.1002/1096-9071(200012)62: 4<450::AID-JMV9>3.0.CO;2-Y]

55 **Rivas P**, Herrero MD, Puente S, Ramírez-Olivencia G, Soriano V. Immunizations in HIV-infected adults. *AIDS Rev* 2007; **9**: 173-187 [PMID: 17982942]

56 **Marcellin P**, Pequignot F, Delarocque-Astagneau E, Zarski JP, Ganne N, Hillon P, Antona D, Bovet M, Mechain M, Asselah T, Desenclos JC, Jougla E. Mortality related to chronic hepatitis B and chronic hepatitis C in France: evidence for the role of HIV coinfection and alcohol consumption. *J Hepatol* 2008; **48**: 200-207 [PMID: 18086507 DOI: 10.1016/j.jhep.2007.09.010]

57 **Vento S**, Garofano T, Renzini C, Cainelli F, Casali F, Ghironzi G, Ferraro T, Concia E. Fulminant hepatitis associated with hepatitis A virus superinfection in patients with chronic hepatitis C. *N Engl J Med* 1998; **338**: 286-290 [PMID: 9445408 DOI: 10.1056/NEJM199801293380503]

58 **Shim M**, Khaykis I, Park J, Bini EJ. Susceptibility to hepatitis A in patients with chronic liver disease due to hepatitis C virus infection: missed opportunities for vaccination. *Hepatology* 2005; **42**: 688-695 [PMID: 16104047 DOI: 10.1002/hep.20830]

59 **European Association For The Study Of The Liver;** European Organisation For Research And Treatment Of Cancer. EASL-EORTC clinical practice guidelines: management of hepatocellular carcinoma. *J Hepatol* 2012; **56**: 908-943 [PMID: 22424438]

60 **Soriano V**, Puoti M, Peters M, Benhamou Y, Sulkowski M, Zoulim F, Mauss S, Rockstroh J. Care of HIV patients with chronic hepatitis B: updated recommendations from the HIV-Hepatitis B Virus International Panel. *AIDS* 2008; **22**: 1399-1410 [PMID: 18614862 DOI: 10.1097/QAD.0b013e3282f8b46f]

61 **Piroth L**, Sène D, Pol S, Goderel I, Lacombe K, Martha B, Rey D, Loustau-Ratti V, Bergmann JF, Pialoux G, Gervais A, Lascoux-Combe C, Carrat F, Cacoub P. Epidemiology, diagnosis and treatment of chronic hepatitis B in HIV-infected patients (EPIB 2005 STUDY). *AIDS* 2007; **21**: 1323-1331 [PMID: 17545709 DOI: 10.1097/QAD.0b013e32810c8bcf]

62 **Lacombe K**, Boyd A, Lavocat F, Pichoud C, Gozlan J, Miailhes P, Lascoux-Combe C, Vernet G, Girard PM, Zoulim F. High incidence of treatment-induced and vaccine-escape hepatitis B virus mutants among human immunodeficiency virus/hepatitis B-infected patients. *Hepatology* 2013; **58**: 912-922 [PMID: 23468093 DOI: 10.1002/hep.26374]

63 **Tenney DJ**, Rose RE, Baldick CJ, Pokornowski KA, Eggers BJ, Fang J, Wichroski MJ, Xu D, Yang J, Wilber RB, Colonno RJ. Long-term monitoring shows hepatitis B virus resistance to entecavir in nucleoside-naïve patients is rare through 5 years of therapy. *Hepatology* 2009; **49**: 1503-1514 [PMID: 19280622 DOI: 10.1002/hep.22841]

64 **Price H**, Dunn D, Pillay D, Bani-Sadr F, de Vries-Sluijs T, Jain MK, Kuzushita N, Mauss S, Núñez M, Nüesch R, Peters M, Reiberger T, Stephan C, Tan L, Gilson R. Suppression of HBV by tenofovir in HBV/HIV coinfected patients: a systematic review and meta-analysis. *PLoS One* 2013; **8**: e68152 [PMID: 23874527 DOI: 10.1371/journal.pone.0068152]

65 **Kitrinos KM**, Corsa A, Liu Y, Flaherty J, Snow-Lampart A, Marcellin P, Borroto-Esoda K, Miller MD. No detectable resistance to tenofovir disoproxil fumarate after 6 years of therapy in patients with chronic hepatitis B. *Hepatology* 2014; **59**: 434-442 [PMID: 23939953]

66 **Di Martino V**, Thevenot T, Colin JF, Boyer N, Martinot M, Degos F, Coulaud JP, Vilde JL, Vachon F, Degott C, Valla D, Marcellin P. Influence of HIV infection on the response to interferon therapy and the long-term outcome of chronic hepatitis B. *Gastroenterology* 2002; **123**: 1812-1822 [PMID: 12454838 DOI: 10.1053/gast.2002.37061]

67 **Marcellin P**, Lau GK, Bonino F, Farci P, Hadziyannis S, Jin R, Lu ZM, Piratvisuth T, Germanidis G, Yurdaydin C, Diago M, Gurel S, Lai MY, Button P, Pluck N. Peginterferon alfa-2a alone, lamivudine alone, and the two in combination in patients with HBeAg-negative chronic hepatitis B. *N Engl J Med* 2004; **351**: 1206-1217 [PMID: 15371578 DOI: 10.1056/NEJMoa040431]

68 **Papatheodoridis GV**. Why do I treat HBeAg-negative chronic hepatitis B patients with nucleos(t)ide analogues? *Liver Int* 2013; **33** Suppl 1: 151-156 [PMID: 23286859 DOI: 10.1111/liv.12054]

69 **Soriano V**, Vispo E, Labarga P, Medrano J, Barreiro P. Viral hepatitis and HIV co-infection. *Antiviral Res* 2010; **85**: 303-315 [PMID: 19887087 DOI: 10.1016/j.antiviral.2009.10.021]

70 **Soriano V**, Tuma P, Vispo E, Labarga P, Fernández JV, Medrano J, Barreiro P. Hepatitis B in HIV patients: what is the current treatment and what are the challenges? *J HIV Ther* 2009; **14**: 13-18 [PMID: 19731560]

71 **Benhamou Y**, Fleury H, Trimoulet P, Pellegrin I, Urbinelli R, Katlama C, Rozenbaum W, Le Teuff G, Trylesinski A, Piketty C. Anti-hepatitis B virus efficacy of tenofovir disoproxil fumarate in HIV-infected patients. *Hepatology* 2006; **43**: 548-555 [PMID: 16496322 DOI: 10.1002/hep.21055]

72 **Zoutendijk R**, Zaaijer HL, de Vries-Sluijs TE, Reijnders JG, Mulder JW, Kroon FP, Richter C, van der Eijk AA, Sonneveld MJ, Hansen BE, de Man RA, van der Ende ME, Janssen HL. Hepatitis B surface antigen declines and clearance during long-term tenofovir therapy in patients coinfected with HBV and HIV. *J Infect Dis* 2012; **206**: 974-980 [PMID: 22782950 DOI: 10.1093/infdis/jis439]

73 **Hughes SA**, Wedemeyer H, Harrison PM. Hepatitis delta virus. *Lancet* 2011; **378**: 73-85 [PMID: 21511329 DOI: 10.1016/S0140-6736(10)61931-9]

74 **Yurdaydın C**, Idilman R, Bozkaya H, Bozdayi AM. Natural history and treatment of chronic delta hepatitis. *J Viral Hepat* 2010; **17**: 749-756 [PMID: 20723036 DOI: 10.1111/j.1365-2893.2010.01353.x]

75 **Soriano V**, Grint D, d'Arminio Monforte A, Horban A, Leen C, Poveda E, Antunes F, de Wit S, Lundgren J, Rockstroh J, Peters L. Hepatitis delta in HIV-infected individuals in Europe. *AIDS* 2011; **25**: 1987-1992 [PMID: 21857493 DOI: 10.1097/QAD.0b013e32834babb3]

76 **Sheldon J**, Ramos B, Toro C, Ríos P, Martínez-Alarcón J, Bottecchia M, Romero M, Garcia-Samaniego J, Soriano V. Does treatment of hepatitis B virus (HBV) infection reduce hepatitis delta virus (HDV) replication in HIV-HBV-HDV-coinfected patients? *Antivir Ther* 2008; **13**: 97-102 [PMID: 18389903]

77 **Matthews GV**, Seaberg EC, Avihingsanon A, Bowden S, Dore GJ, Lewin SR, Sasadeusz J, Revill PA, Littlejohn M, Hoy JF, Finlayson R, Ruxrungtham K, Saulynas M, Locarnini S, Thio CL. Patterns and causes of suboptimal response to tenofovir-based therapy in individuals coinfected with HIV and hepatitis B virus. *Clin Infect Dis* 2013; **56**: e87-e94 [PMID: 23315316 DOI: 10.1093/cid/cit002]

78 **Hongthanakorn C**, Chotiyaputta W, Oberhelman K, Fontana RJ, Marrero JA, Licari T, Lok AS. Virological breakthrough and resistance in patients with chronic hepatitis B receiving nucleos(t)ide analogues in clinical practice. *Hepatology* 2011; **53**: 1854-1863 [PMID: 21618260 DOI: 10.1002/hep.24318]

79 **Altfeld M**, Rockstroh JK, Addo M, Kupfer B, Pult I, Will H, Spengler U. Reactivation of hepatitis B in a long-term anti-HBs-positive patient with AIDS following lamivudine withdrawal. *J Hepatol* 1998; **29**: 306-309 [PMID: 9722213 DOI: 10.1016/S0168-8278(98)80017-2]

80 **Miailhes P,** Maynard-Muet M, Lebossé F, Carrat F, Bouix C, Lascoux-Combe C, Sogni P, Rey D, Barthe Y, Pol S, Cacoub P, Zoulim F, Piroth L. Role of a 48-week pegylated interferon therapy in hepatitis B e antigen positive HIV-co-infected patients on cART including tenofovir: EMVIPEG study. *J Hepatol* 2014; Epub ahead of print [PMID: 24882048 DOI: 10.1016/j.jhep.2014.05.030]

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Table 1 immunogenicity of 4 intramuscular double doses and 4 intradermal low doses *vs* standard hepatitis B vaccine regimen in adults with human immunodeficiency virus[53]

|  |  |  |  |
| --- | --- | --- | --- |
| ***n =* 426** | **IM 20 μg x 3**  ***n =* 141** | **im 40 μg x 4**  ***n =* 145** | **id 4 μg x 4**  ***n =* 140** |
| **Response rates**  **At week 28**  **(Anti-HBs > 10 mIU/ml)** | 65%  95%CI: 56%-72% | 82%  95%CI: 77%-88%  *P* < 0.001 *vs* IM 20 x 3 | 77%  95%CI: 69%-84%  *p* = 0.02 *vs* IM 20 x 3 |
| **High responders rates**  **(Anti-HBs > 100 mIU/ml)** | 41%  95%CI: 33%-50% | 74%  95%CI: 66%-81%  *p* < 0.001 *vs* IM 20 x 3 | 53%  95%CI: 44%-61%  *p* = 0.06 *vs* IM 20 x 3 |

anti-HBs: antibody to hepatitis B antigen.