
# European AIDS Clinical Society (EACS)

# Guidelines for the clinical management and treatment of chronic hepatitis B and C coinfection in HIV-infected adults

These Euroguidelines result from the 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, the updated recommendations from the HCV-HIV International Panel (Soriano V, Puoti M, Sulkowski M, Cargnel A, Benhamou Y, Peters M, Mauss S, Bräu N, Hatzakis A, Pol S, Rockstroh J. Care of patients coinfected with HIV and hepatitis C virus: 2007. AIDS. 2007;21:1073-1089) and from a discussion with the following panel:

## PANEL MEMBERS

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# General recommendations for counseling in patients with HIV and hepatitis coinfection

SCREENING

1. All HIV-infected patients should be screened for hepatitis C at diagnosis and then on an annual basis. Screening for HCV in HIV-infected patients should be done using a third generation anti-HCV antibody test. A positive result should be followed by evaluation for the presence of HCV-RNA and the genotype should be determined. Patients with risk factors (ongoing IVDU, mucosal traumatic sex ;consider recent outbreak of acute HCV in msm) with unexplained increase in hepatic transaminases and a negative HCV antibody test should be offered an HCV-RNA test for early detection of a recent infection.
2. HIV-infected patients should be screened for hepatitis A and B.
3. Hepatitis delta antibodies should be screened for in all HBsAg+ patients.

VACCINATION

4. Patients lacking anti-HAV IgG-antibodies and anti-HBV antibodies should be offered vaccination for the respective virus to prevent infection regardless of their CD4-count. The response to the vaccine is influenced by the CD4-count and level of HIV-RNA. In patients with low CD4-counts (< 200/µl) and ongoing HIV replication, HAART should be initiated first prior to respective vaccination. In case of insufficient response (anti-HBs < 10 IU/l) re-vaccination should be considered. Double dose revaccination (40µg) at 3-4 vaccination time points (month 0, 1, 6 and 12) may help to improve response rates to vaccination.

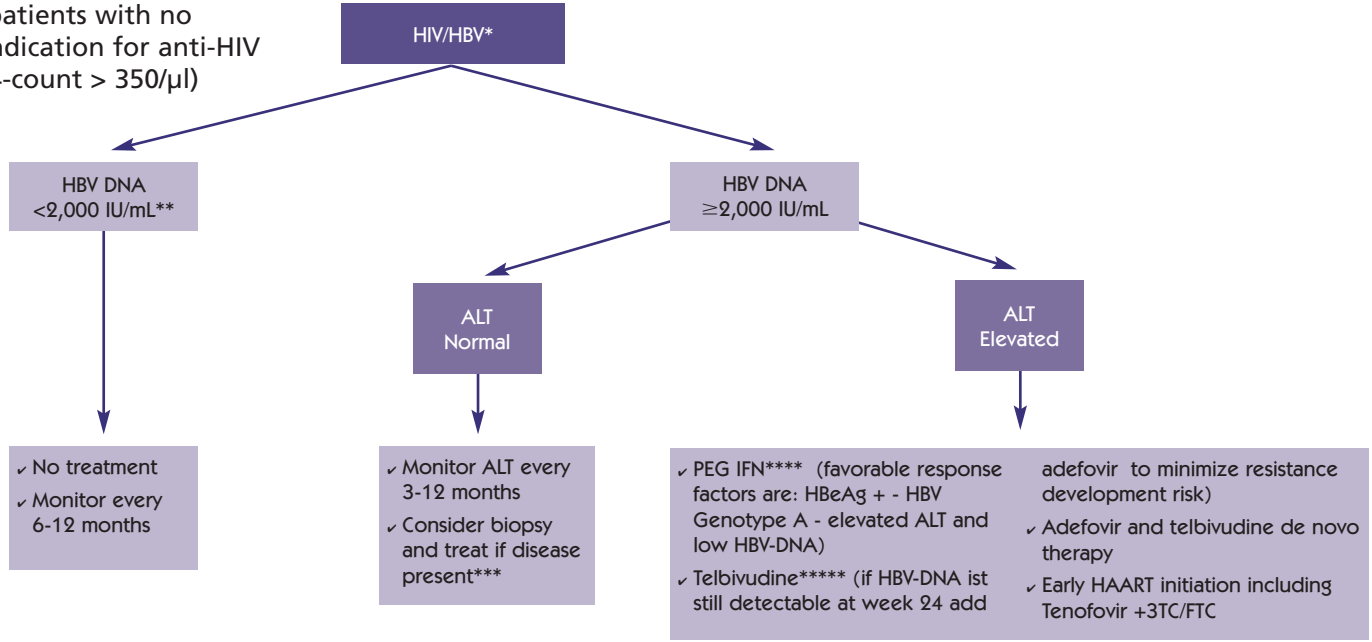
   Patients who failed to seroconvert after hepatitis B vaccination and remain at risk for HBV-infection should be monitored annually for serological markers of HBV-infection.

PREVENTION/SUPPORT

5. Psychological, social and medical support should be made available to stop patients with a high alcohol intake from drinking or to strongly advise them to limit alcohol consumption.
6. Substitution therapy (opioid replacement therapy) in patients with active drug abuse as a step towards cessation of active drug use should be considered; help provided (e.g. through needle- and syringe-exchange programs) reduces the risk of reinfection including parenteral viral transmission (harm reduction strategy).
7. Since HBV and HIV and occasionally HCV are transmitted sexually, adequate counseling including the use of condoms is advisable. Mucosal traumatic sexual practices associated with a high risk of blood contact should be forbidden.

**Figure 1:**

Management and therapeutic options in compensated HBV/HIV co-infected patients with no immediate indication for anti-HIV therapy (CD4-count > 350/µl)




* chronic HBV-infection defined as HBsAg+ > 6 months.

** Serum HBV-DNA levels have been demonstrated to be associated with a linear increased risk for development of liver cirrhosis and HCC; please note that the calculation from copies to IU/ml varies depending on which respective test assay was used; in general 1 IU/ml equals around 5 copies or genome equivalents; one picogram HBV-DNA equals 2,8x10$^5$ genome/ml.

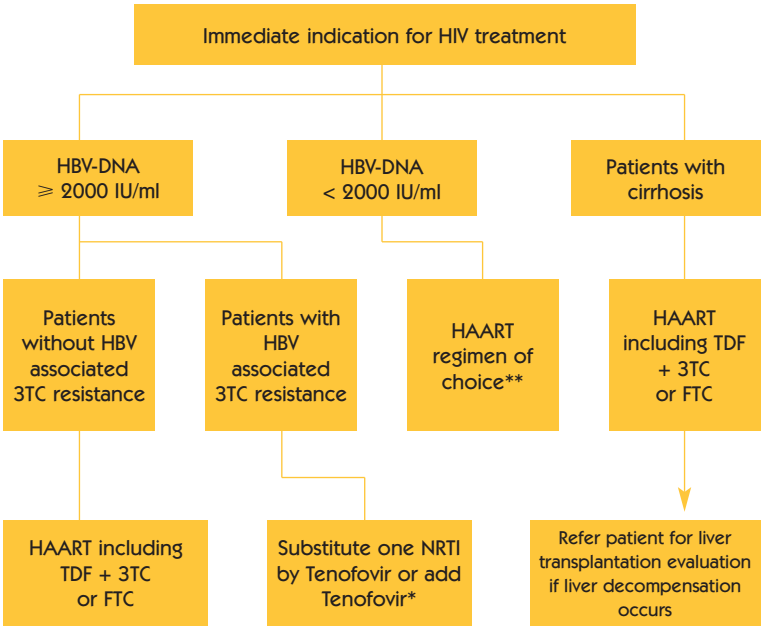
*** Metavir ≥ A2 and/or F2; Patients with replicating HBV and normal liver enzymes may have significant liver damage, therefore consider assessment of liver damage; this may be done using either liver biopsy or non-invasive tools, including serum fibrosis markers or fibroScan. While liver biopsy may provide additional information on inflammation and other lesions (e.g., steatosis), non-invasive markers can be used at more frequent intervals.

**** treatment length: 48 weeks for PEG INF; for the nucleoside analogues: HBsAg seroconversion + 6 mths. In those not requiring HAART and on treatment with telbivudine +/- adefovir, or those on HAART where nucleoside back-bone needs changing, anti-HBV therapy may be stopped cautiously in HBeAg+ patients who have achieved HBe-seroconversion or HBs-seroconversion for at least six months or, after HBs-seroconversion for at least six months in those who are HBeAg-.

***** So far only licensed in the US and selected European countries.

**Figure 2:**

Management and therapeutic options in compensated or cirrhotic HBV/HIV co-infected patients with an indication for HIV treatment (CD4-count ⩽ 350/µl or already on HAART)




* if feasible and appropriate from the perspective of maintaining HIV suppression
In some cases of tenofovir intolerance (i.e. renal disease), entecavir 1 mg/day may be advisable.

** some experts strongly think that any HBV-infected patient requiring HAART should receive TDF +3TC or FTC unless history of TDF intolerance

**Table 1:**

Treatment recommendations for therapy of hepatitis C in HIV coinfection

1. HCV treatment offers the possibility of eradicating HCV within a defined treatment period. This is potentially advantageous for the subsequent management of the patient with HIV, and every patient should therefore be considered for treatment when the benefits of therapy outweigh the risks. This also needs to be seen in the context of faster liver fibrosis progression in HIV/HCV coinfection and with better HCV treatment outcome with improved management in these patients.

2. Information on liver fibrosis staging is important for making therapeutic decisions in coinfected patients. However, a liver biopsy is not mandatory for considering treatment of chronic HCV. Current therapy is particularly recommended in patients with a high likelihood of achieving sustained virological response (SVR): genotype 2 or 3 and patients infected with genotype 1 if the viral load is low (<400.000-500.000 IU/ml)

3. In case of the availability of a liver biopsy or Fibroscan demonstrating lower grades of liver fibrosis (F0-1), regardless of HCV genotype, treatment can be deferred. A liver disease stage assessment is especially important to perform in patients with a low chance of SVR.

4. The combination of Peg-IFN-alpha and ribavirin (RBV) is the treatment of choice for HCV infection. The standard dose for Peg-IFN 2a is 180µg once weekly, and for Peg-IFN 2b it is 1.5 µg/kg >>>

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bodyweight once weekly. An initial weight adapted dose of RBV of 1000 (wt < 75kg) -1200 (wt > 75kg) mg daily (administered bid) is recommended for all genotypes.

5. The primary aim of anti-HCV treatment is sustained virological response defined as undetectable serum HCV-RNA 24 weeks after the end of therapy, evaluated using sensitive molecular tests.

6. If chronic hepatitis C is detected early in the course of HIV infection (before the initiation of HAART is necessary), treatment for chronic HCV is advised. However, if a coinfected patient has severe immunodeficiency (CD4 count < 200 cells/µl), the CD4 count should be improved using HAART prior to commencing anti-HCV treatment. Patients with a CD4 relative percentage >25% are more likely to achieve SVR than lower CD4 percentage.

7. If an early virological response of at least 2 log10 reduction in HCV-RNA compared to baseline is not achieved at week 12, treatment should be stopped (figure 3).

8. During Peg-FN plus ribavirin therapy, ddI is contraindicated in patients with cirrhosis and should be avoided in patients with less severe liver disease. D4T and AZT also if possible should be avoided. The role of abacavir is uncertain at this point but cohort data at least suggests lower SVR results in patients receiving abacavir containing HAART.

9. In patients with acute HCV-infection HCV therapy is recommended if the HCV-RNA is confirmed positive (1 week apart) by week 12 post HCV transmission as SVR rates following treatment of acute HCV-infection are higher than for treatment of chronic HCV.

## Table 2:

Diagnostic procedures for hepatitis C in HIV-coinfection

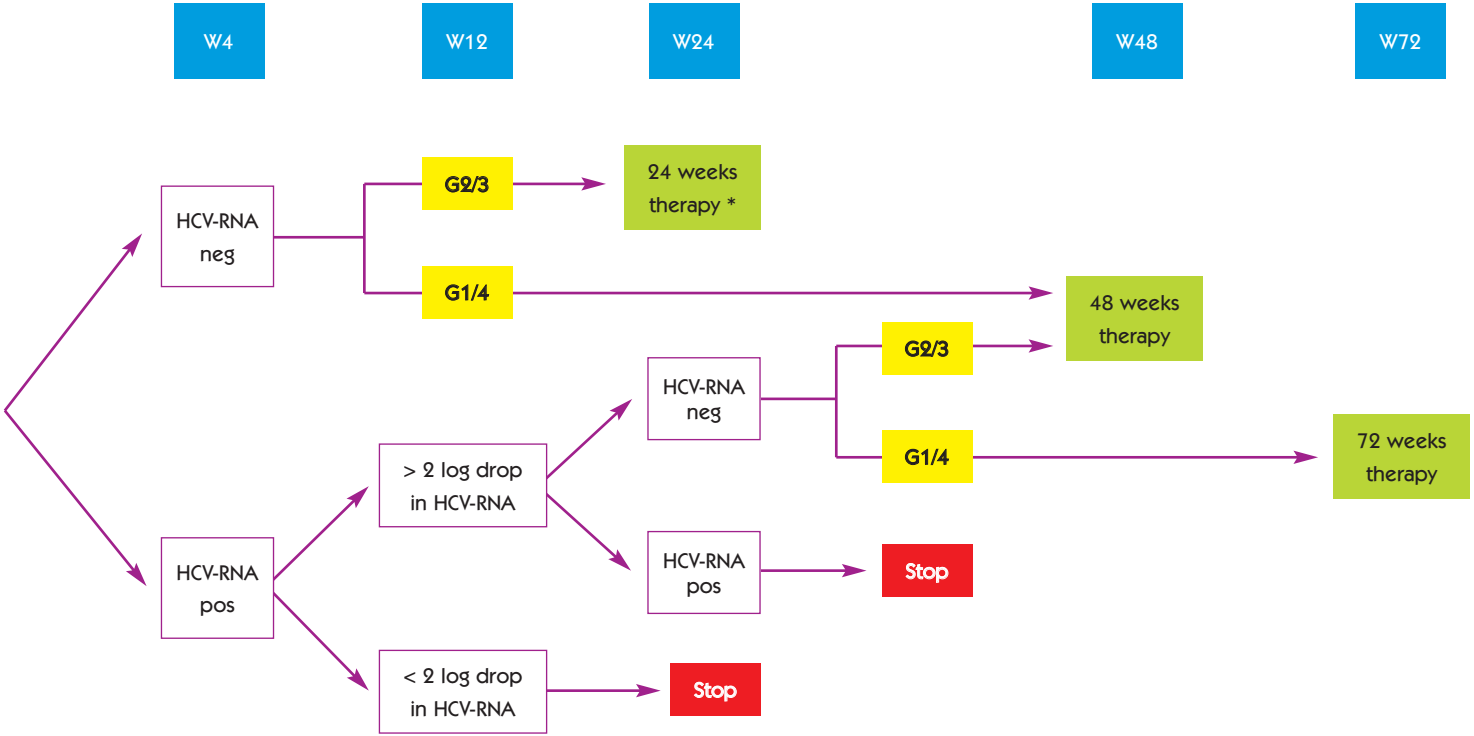
| Diagnosis of hepatitis C |
|---|
| HCV-Ab (positive 1-5 months after infection, may rarely be lost with immunosuppression) |
| HCV-RNA levels* (while not prognostic for progression, it is for response to treatment) |
| **Status of liver damage** |
| Grading of fibrosis (e. g. Fibroscan, liver biopsy, serum fibromarkers**) |
| Hepatic synthetic function (e. g. coagulation, protein, albumin, CHE) |
| Ultrasound and AFP every 6 months in cirrhotics (gastroscopy upon diagnosis of cirrhosis and every 1-2 years thereafter) |
| **Before HCV treatment** |
| HCV genotype and serum HCV-RNA |
| Autoantibodies (ANA, SMA, ANCA and LKM1) |
| TSH, thyroid autoantibodies if applicable; |
| **Monitoring of HCV treatment** |
| Differential blood count and liver enzymes every 2-4 weeks |
| HCV-RNA at week 4 (to evaluate rapid virological response), week 12, 24, 48, (72 if applicable) and 24 weeks after stopping HCV therapy |
| CD4-count every 12 weeks |
| TSH every 12 weeks |

* Low viral load defined as less than 400,000 IU/l when using pegIFN+RBV. There is no standard conversion formula for converting the amount of HCV-RNA reported in copies/ml to the amount reported in IU. The conversion factor ranges from about one to five HCV-RNA copies per IU.

**Serum fibromarkers include APRI, FIB-4, Hyaluronic acid, Fibrotest, Forns and other indexes

**Figure 3:**

Proposed optimal duration of HCV therapy in HCV/HIV-coinfected patients.




* In patients with baseline low viral load (<400 000 IU/l) and minimal liver fibrosis.

**Table 2:**

Classification of and interventions for HCV/HIV-coinfected non-responders/relapsers to prior interferon-based therapies.

| Category | Recommended intervention |
|---|---|
| Suboptimal prior treatment schedules:<br>↙ *Interferon (monotherapy or with ribavirin)*<br>↙ *Low ribavirin doses*<br>↙ *Short length of therapy* | Re-treatment using combination therapy with peginterferon plus weight-based ribavirin doses |
| Limiting toxicities & poor adherence | Optimal support (SSRI, paracetamol/NSAID, pharmacists, use of hematopoietic growth factors) |
| Virological failure | ↙ Maintenance therapy in patients with cirrhosis (Caveat: no data yet in coinfection, no indication in any country)<br>↙ Wait until new antivirals come to the market in the rest |