

## **2008 APASL guidelines for HBV management**

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Since the third version of Asian-Pacific consensus on the management of hepatitis B was published in June 2005, Pegylated interferon  $\alpha$ 2a, entecavir and telbivudine have been approved globally and several updated guidelines on chronic hepatitis B have been published. In addition, large volume of new data on the natural history and treatment of chronic hepatitis B have become available. These include long-term follow-up studies in large community-based cohorts or asymptomatic subjects with chronic hepatitis B virus (HBV) infection, further studies on the role of HBV genotype/naturally occurring HBV mutations, treatment of drug resistance and new therapies. We have since monitored the progress and held a 2-day expert meeting to review and assess relevant new data. The significance of the reported findings were discussed and debated. The earlier APASL “consensus statement on the management of chronic hepatitis B” (Liver Int 2005;25:472-489) was revised accordingly. The key terms used in the statement were also defined. The new APASL guidelines are:

***Recommendation 1. Thorough evaluation and counselling are mandatory before considering drug therapy (II).***

***Recommendation 2. Patients with viral replication but persistently normal or minimally elevated ALT levels should not be treated, except in patients with advanced fibrosis or cirrhosis. They need adequate follow-up and HCC surveillance every 3-6 months (I).***

**Recommendation 3.** *Prior to therapy, liver biopsy is recommended in patients with HBV replication and raised ALT level, or those with high normal ALT and age over 40 (II).*

**Recommendation 4.** *Chronic hepatitis B patients with ALT > 2x ULN and HBV-DNA > 2.0 x10<sup>4</sup> IU/ml (10<sup>5</sup> copies/ml) if HBeAg positive, or > 2.0x10<sup>3</sup> IU/ml (10<sup>4</sup> copies/ml) if HBeAg-negative, should be considered for treatment (I). Treatment should be started as early as possible in case of impending or overt hepatic decompensation (II). Otherwise, 3-6 months observation is recommended (II).*

**Recommendation 5.** *Patients can be treated with conventional IFN 5-10 mu 3x/week or Pegylated IFN- $\alpha$ 2a 90-180  $\mu$ g weekly (I), entecavir 0.5 mg daily (I), adefovir 10 mg daily (I), telbivudine 600 mg daily (I), or lamivudine 100 mg daily (I). Thymosin- $\alpha$  1.6 mg 2x/week can also be used (I). Lamivudine is recommended if there is a concern regarding ensuing or overt hepatic decompensation (II). Entecavir and telbivudine may also be used in this situation (IV).*

**Recommendation 6.** *During therapy, ALT HBeAg and/or HBV-DNA should be monitored at least every 3 months (I). Renal function should be monitored if adefovir is used (I). During interferon therapy, monitoring of adverse effects is mandatory (I).*

**Recommendation 7.** *After the end of therapy, levels of ALT and HBV-DNA should be monitored monthly for the first 3 months to detect early relapse, and*

*then every three months (for cirrhotic patients and those who remain HBeAg/HBV-DNA positive) to six months (for responders) (II). For non-responders, further monitoring of HBV markers is required to recognize a delayed response and to plan retreatment when indicated (II).*

*Recommendation 8. For conventional IFN, the current recommended duration of therapy is 4-6 months for HBeAg positive patients(II) and at least a year for HBeAg negative patients (I). For Peg-IFN, the recommended duration is at least 6 month for HBeAg positive patients (II) , 12 months for HBeAg negative patients (I). For thymosin  $\alpha_1$ , the recommended duration of therapy is 6 months for both HBeAg positive (I) and negative patients (II).*

*Recommendation 9. For oral antiviral agents: In HBeAg positive patients, treatment can be stopped when HBeAg seroconversion with undetectable HBV-DNA has been documented on two separate occasions at least 6 months apart (II). In HBeAg negative patients, it is not clear how long treatment should be continued, but treatment discontinuation can be considered if undetectable HBV-DNA has been documented on three separate occasions 6 months apart. (II).*

*Recommendation 10. For female patients of child-bearing age, IFN-based therapy is preferred for nonpregnant women and pregnancy is discouraged during IFN-therapy. Women who become pregnant while on oral antiviral drug(s) can continue treatment with category B drug(s) (VI).*

*Recommendation 11. Adefovir, telbivudine or interferon (if  $CD_4 > 500$ ) is preferred if patient's HIV infection does not require treatment. If patient's HIV infection requires treatment, tenofovir or lamivudine/tenofovir combination should be included in the active antiretroviral therapy (II).*

*Recommendation 12. In patients with concurrent HCV or HDV infection, determine which virus is dominant and treat the patients accordingly (III)*

*Recommendation 13. Lamivudine is the agents of choice for treatment naïve patients with obvious or impending hepatic decompensation (II). Entecavir and telbivudine can also be used (III).*

*Recommendation 14. Before receiving immunosuppression or chemotherapy, patients should be screened for HBsAg (III). If HBsAg is positive, prophylactic therapy with a direct antiviral agent before the start and up to at least 12 weeks after the end of immunosuppression or chemotherapy is recommended (I).*

*Recommendation 15. For patients who developed drug resistance while on lamivudine, add-on adefovir therapy is indicated (I), switching to entecavir (1mg/day) is an option (I). For lamivudine naïve patients who developed drug resistance while on adefovir, add-on or switching to lamivudine, telbivudine or entecavir is indicated (III). For patients who developed drug resistance while on telbivudine, add-*

*on adefovir therapy is indicated (IV). Switching to IFN based therapy is an option (III)*

*Recommendation 16-1. Nucleos(t)ide analogue(s) should be commenced in all patients with HBV-associated liver failure who are listed for transplantation and have detectable HBV-DNA. Lamivudine plus low dose HBIG (400-800 U, i.m. daily for 1 week, followed by 400-800 U monthly long term) provide safe and effective prophylaxis against HBV reinfection of the allograft (II). Alternatively, lamivudine + adefovir prophylaxis can be considered (II)*

*Recommendation 16-2. Late conversion (at least 12 months post-transplant) HBIG substitution by adefovir provides safe and cost-effective prophylaxis (II). Late conversion to lamivudine mono-therapy may be considered in “low-risk” patients (I).*

*Recommendation 16-3. HBV-naïve patient receiving a liver from anti-HBc (+) donor should receive long-term prophylaxis with either Lamivudine or HBIG (III).*