Recent advances for the treatment of chronic hepatitis B

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Hepatitis B virus (HBV) infection is a major health concern which causes about one million deaths annually worldwide. A wide range of clinical manifestations have been established for chronic HBV infection, from asymptomatic carriers to severe chronic liver disease, including those with cirrhosis and hepatocellular carcinoma (HCC). Peginterferon and oral nucleos(t)ide analogs (NAs) (lamivudine, adefovir, telbivudine, entecavir and tenofovir) are used in the treatment of chronic hepatitis B (CHB) patients, which are very effective in viral suppression and normalization of liver enzymes.

Peginterferon α (PEG-IFN) can be used to treat patients with CHB infection. A finite duration of PEG-IFN therapy may lead to long-term viral suppression. Clinically, it is important to identify super-responders and null-responders to PEG-IFN due to its substantial side effects. From the literature review, it is known that PEG-IFN is more effective for hepatitis B e antigen (HBeAg)-positive patients who have high pre-treatment ALT level, lower HBV DNA level and genotype A, as well as those with more favourable viral predictors. For HBeAg-positive and -negative patients, PEG-IFN therapy could be terminated early at week 12 or 24 in primary nonresponders defined by the HBsAg stopping rules.

Previous studies have indicated that entecavir and tenofovir therapy has proved to be a highly efficacious and low resistance-conferring agent in NA-naïve patients. However, entecavir monotherapy may not be the optimal rescue therapy in patients with a prior history of lamivudine-resistant mutants. Entecavir therapy did not completely eliminate HCC risk, but significantly reduced HCC incidence compared with untreated controls. The selection between entecavir and lamivudine treatment may not be an independent predictor for mortality in CHB patients with acute exacerbation and hepatic decompensation. HBsAg levels might be useful predictors to guide the timing of cessation of entecavir treatment in CHB patients. Tenofovir monotherapy maintains effective suppression of HBV DNA through 6 years of treatment with no evidence of tenofovir resistance. Tenofovir alone is as effective as emtricitabine/tenofovir for treatment of patients with lamivudine-resistant mutants and suboptimal response to adefovir. In HBeAg(+) patients with chronic HBV infection, high viral loads, normal levels of ALT, and therapy with the combination of tenofovir and emtricitabine provided better viral suppression than tenofovir alone.

However, the rates of HBeAg loss/seroconversion and HBsAg loss were low after 4 years of treatment. Long-term telbivudine therapy was associated with a sustained improvement of renal function—particularly among patients with increased risk of renal impairment.