Optimizing Current Therapy in Asian Patients: Update in Peg-IFN Therapy

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Pegylated interferon (PegIFN) is one of the first line therapy for chronic hepatitis B. A 48-week PegIFN therapy achieves sustained response in 33% and 24% in HBsAg-positive and HBeAg-negative chronic hepatitis B, respectively. Baseline and response guided-therapy has been reported to improve treatment response. Lower HBV DNA level, higher serum ALT, HBV genotype A, B and lower HBsAg level at baseline are associated with better response to PegIFN therapy. Patients with baseline ALT >5 times of ULN and HBV DNA lower than 10 log copies/ml achieved HBeAgseroconversion in 52% comparing with 32% in those with lower baseline ALT and high HBV DNA levels. On treatment predictors of response to PegIFN therapy include serum HBV DNA level, ALT flare, HBsAg level or HBsAg decline. Patients achieving a decline HBsAg of more than 0.5 log IU/ml within 4 weeks after ALT flare would have HBsAg loss in 64%. LowerHBsAg levels at treatment week12or week24 is associated with better treatment response (55% HBeAgseroconversion and 11% HBsAg loss in those with HBsAg level less than 1,500 IU/ml at treatment week12 or week24). HBsAg level above 20,000 IU/ml at treatment week 24 is associated with very low HBeAg loss and HBV DNA <2,000 IU/ml providing negative predictive value of 97% and can be used as stopping rule for HBeAg-positive chronic hepatitis B in all HBV genotypes. Extended PegIFN treatment duration has been reported with improved response in patients with partial response to 48-week PegIFN therapy. In patients with HBeAg-negative chronic hepatitis B, HBsAg decline more than 10% at treatment week12 or week24 had sustained virological response with HBV DNA <20,000 IU/ml in 42% and HBsAg loss in 22% at 5-year post-treatment. Extended PegIFN treatment to 96 weeks significantly improves sustained responseupto 80% of those who achieved more than 10% HBsAg decline at treatment week12 or week24. No HBsAg decline at week 12 in combination with less than 2 logs decline of HBV DNA level provide negative predictive value of 100% and can be used as stopping rule in HBeAg-negative chronic hepatitis B

Recent studies have demonstrated benefit of PegIFN and nucleos(t)ide analogue combination therapy in chronic hepatitis B patients. Switching to PegIFNin HBeAg-positive chronic hepatitis B,who achieved HBV DNA less than 1,000 copies/mlafter 12 weeks of entecavir therapy, has better HBeAgseroconversion and HBsAg loss than entecavirmonotherapy. HBsAglevel less than 1,500 IU/ml at the time of switching therapy is associated with high rate ofHBsAg loss of 22%. Sequential therapy with PegIFN after 12-week entecavir also showed good virological and serological response in HBeAg positive patients who achieved more than half a log decline at week12.Recent study of tenofovir and PegIFN de novo combination therapy showed higher rates of HBsAg loss than PegIFN or tenofovirmonotherapy.

In conclusion, baseline and on-treatment response guided-therapy can optimize PegIFN therapy in chronic hepatitis B. PegIFN and NAs combination therapy is promising strategy. However, further study to identify the right patients and combination strategy is required.