DAA/PR therapy in Asian HCV patients

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Chronic hepatitis C virus (HCV) infection is one of the leading causes of liver decompensation and hepatocellular carcinoma. Patients with genotype 1 HCV generally show poor response to peg-interferon plus ribavirin therapy. However, the eradication rate has improved greatly with the advent of protease inhibitors. The first generation protease inhibitors (PIs) telaprevir and boceprevir were the first direct acting anti-viral agents (DAAs) to be approved for treatment of HCV genotype 1. Despite the improved eradication rates, adverse events associated with peg-interferon plus ribavirin plus telaprevir/boceprevir triple combination therapy, including anemia, appetite loss, and skin rash may be very severe and require drastic ribavirin dose reduction and/or discontinuation of one more of the therapy drugs and consultation with a dermatologist. A second wave of first generation PIs, such as simeprevir and vaniprevir, have much better anti-viral effects as well asfewer side effects than were observed with the first wave drugs, although the side effects associated with peg-interferon and ribavirin remain an issue and limit treatment eligibility in some patients. More recent development of second generation PIs, such as MK-5172 and ACH-2684, and new classes of DAA targeting other viral proteins, including NS5A inhibitors, such as daclatasvir and ombitasvir, and polymerase inhibitors, such as sofosbuvir and beclabuvir (BMS-791325), have enabled us to avoid peg-interferon and ribavirin in favor of interferon-free DAA combination therapies while still maintaining high eradication rates. The reduced side effects and shorter duration of interferon-free DAA therapy has also improved patient eligibility, especially among patients with cirrhosis or prior non-response to interferon therapy. DAA therapies with pan-genotypic efficacy are also being developed to treat other HCV genotypes. For these reasons, peg-interferon has already been removed from the AASLD treatment guidelines. However, peg-interferon and ribavirin with or without DAA must still be used to treat patients who develop rapidly progressing chronic hepatitis with high ALT levels before DAA-only therapy can be initiated. Another possible role for peg-interferon plus ribavirin therapy might be to treat patients who develop resistance against multiple drugs. Although the long-term consequences of DAA resistance are not yet clear, patients who have developed resistance against both PIs and NS5A inhibitors have been reported, and the possibility of resistance to all three major DAA classes has been reported. I will take this opportunity to describe the evolving role of peg-interferon plus ribavirin with protease inhibitors in treatment of HCV in Asian patients and discuss possible applications of this therapy in the future.