IFN-free therapy

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The progress of DAA in HCV treatment is moving from IFN (IFN)-containing regimens in 2011 to IFN-free regimens in 2013, which are currently standard-of-care in most Western countries. There are many DAA regimens expected come to the Asia-Pacific. Notably, the variety and uncertainty of timeline for DAAs to Asia-Pacific make the difficulty of a universal HCV practice guideline fitting the whole Asian population. However, emerging progress of potent DAAs with high genetic barriers and safety profiles have provided much more chance of DAA IFN-free regimens available in he near future.

Sofosbuvir plus weight-based dose of RBV, the first IFN-free regimen, is approved for all HCV genotypes in Australia and Macau in 2014. With 12-week and 24-week regimens for HCV-2 and HCV-3 patients, respectively, the SVR rates could reach > 90%. However, 24-week sofosbuvir/RBV, with SVR rate of 60%-70% for HCV-1 patients, is an alternative recommendation for IFN-ineligible patients. Instead, 12-week sofosbuvir plus simeprevir, with high SVR rates (>90%) in phase 2 COSMOS trial, is an off-label recommendation for HCV-1/4-6 IFN-ineligible patients. The first approved IFN-free regimen for HCV-1b, 24-week daclatasvir plus asunaprevir (NS3/4A protease inhibitor), is approved in Japan, July 2014, for IFN-ineligible/intolerant and treatment-experienced patients with SVR rates of 85%-90%. Sofosbuvir plus daclatasvir with/without RBV for 12-24 weeks is approved for naïve or experienced HCV1-4 patients in Europe, August 2014. A fixed-dose combination of sofosbuvir/ledipasvir, a NS5A inhibitor, for 8-12 weeks with SVR rates of >92% for HCV-1 naive and experienced patients is approved in US, October 2014. Both regimens are expected to be available in Asia-Pacific before 2016. A 3-DAA (co-formulated ABT-450/r [Ns3/4A protease inhibitor boosted by ritonavir]/Ombitasvir [NS5A inhibitor] and Dasabuvir [NS5B non-nucleoside analogue]) plus RBV for 12 weeks achieved high SVR rates (90%-95%) for naïve/experienced, cirrhotic/non-cirrhotic HCV-1 patients in phase 3 trials. A 12-week 3-DAA regimen for HCV G1b non-cirrhotics and a 12-week 3-DAA/RBV regimen for HCV G1a and cirrhotic HCV G1b patients are approved in December 2014. Soon later, another fixed-dose combination of 3-DAA (daclatasvir/asunaprevir/beclauvir) for HCV G1 and a 2-DAA (Grazoprevir/Elbasvir) for HCV G1/4 might get the approval after phase 3 studies confirming the efficacy and safety.

Lacking “one size fits all” regimen increases the HCV treatment barriers. The current recommendation should be based on the availability, indication and cost-effectiveness of DAAs in Asia-Pacific. In the emerging era of DAA, treatment should weigh the benefit/risk and cost-effectiveness, especially in lower socioeconomic areas of Asia-Pacific. It is therefore PegIFN/RBV will hang around for a couple of years in Asia-Pacific countries before effective and affordable IFN-free DAA regimens become available.