Overview of Directly Acting Antiviral Agents for HCV

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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 and are expected come to the Asia-Pacific soon later.

IFN-containing regimens: The first-wave of NS3/4A protease inhibitors, boceprevir and telaprevir, in combination with PegIFN/RBV for 24-48 weeks based on RGT have been approved for HCV-1 treatment-naïve and experienced patients in several Asia-Pacific countries since 2011. However, adding protease inhibitor had no benefit for HCV-1 naïve patients with LVL and RVR with 24-week PegIFN/RBV. Japan recently approves 24-week telaprevir triple therapy for HCV-2 in September 2014. Simeprevir, a second-wave of protease inhibitor, once-daily dosing with better safety profile, is approved in Japan September 2013 and Australia recently: 12-week simeprevir/PegIFN/RBV triple therapy plus 12-week and 36-week PegIFN/RBV for HCV-1/4 naïve and experienced patients, respectively. Sofosbuvir, a pangenotypic NS5B nucleotide polymerase inhibitor, once-daily dosing with superior safety profiles and high treatment efficacy (>90%), is approved recently in Australia and Macau: 12-week sofosbuvir plus PegIFN/RBV for naïve or experienced HCV1/3-6 patients. Daclatasvir, a NS5A inhibitor, in combination with PegIFN/RBV based on RGT is approved for HCV-4 patients in Europe, October 2014.

IFN-free regimens: 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 (asunaprevir/daclatasvir/beclabuvir) 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.