Direct-acting antivirals: The answer to hepatitis C virus reactivation after organ transplantation?

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Hepatitis C virus (HCV) infection and/or reactivation are dreadful conditions in patients post-organ transplantation, which are among the leading causes of death and allograft loss.[1] Immunosuppression after transplantation is the major risk factor for HCV infection/reactivation and anti-viral treatment is mandatory. Unfortunately, although pegylated interferon, with or without ribavirin, has been used to treat recipients with HCV infection post-organ transplantation, interferon-based therapy is contraindicated in patients with liver decompensation and the treatment is often subject to dose reduction or discontinuation due to threatening and undesirable side effects. Furthermore, the response rate is only suboptimal. Therefore, HCV reactivation/infection after organ transplantation have been difficult to treat, until the introduction of direct antiviral agents (DAAs). DAAs are pharmacological agents attacking crucial points in the life cycle of HCV. They are molecules that target specific nonstructural proteins of the virus, leading to disruption of viral replication and infection. DAAs have aroused much attention because of the excellent safety profiles and success rates as compared with interferon-based therapies. However, the data of their application for Asian patients with HCV infection post-organ transplantation are up to now, still quite limited.

In the past few years, some studies have addressed the promising results of DAA treatment for patients with HCV infection post-organ transplantation. The ALLY-1 study[2] reported the treatment efficacy of daclatasvir, sofosbuvir, and ribavirin with a 24-week follow-up in two cohorts of patients with chronic HCV infection of any genotype and either compensated/decompensated cirrhosis or post-transplantation recurrence. Among the study subjects, 55% had advanced fibrosis or cirrhosis. A total of 53 patients with genotype 1a (58%), 1b (19%), and 3 (21%) were treated with daclatasvir (60 mg/day), sofosbuvir (400 mg/day), and ribavirin. Sustained virologic response (SVR)12 was noted in 95% and 91% of patients with genotype 1 and 3 infections, respectively. The authors concluded that the pan-genotypic combination of daclatasvir, sofosbuvir, and ribavirin have yielded high SVR rates across multiple HCV genotypes in patients with post-liver transplantation recurrence or advanced cirrhosis. The results of the SOLAR studies[3,4] are also worth noting: post-transplant patients with genotype 1 or 4 HCV infection (and also those with end-stage liver disease) were enrolled. In the SOLAR-1 study,[3] the cohort B recruited post-transplant patients that were non-cirrhotic (n = 111) or cirrhotic with various degrees of liver dysfunction (Child-Pugh class A, n = 51; class B, n = 52; class C, n = 9). Sofosbuvir and ledipasvir treatment for 12 weeks achieved an SVR12 of 96%, 98%, 86%, and 60%, respectively. The SOLAR-2 study was on the other hand conducted in Europe, Canada, and New Zealand[4] with the patients being non-cirrhotic (n = 89) or cirrhotic (Child-Pugh class A, n = 58; class B, n = 40; and class C, n = 7, excluding those with the Child-Pugh score higher than 13). Sofosbuvir, ledipasvir, and ribavirin treatment for 12 weeks achieved SVR12 of 93%, 100%, 95%, and 50%, respectively. Furthermore, the AMBER-CEE study[5] found that ombitasvir, paritaprevir-ritonavir, and dasabuvir treatment with or without ribavirin for 35 liver transplant recipients with recurrent HCV genotype 1 infection (91% genotype 1b, 77% at fibrosis stage ≥ F2) exerted a SVR12 of 100%. Excellent virologic responses were noted, irrespective of prior treatment history or the degree of fibrosis. Regarding daclatasvir-based regimens, a Spanish multicenter study[6] disclosed that, in 331 post-transplant patients (49% with advanced fibrosis, F4) receiving anti-HCV treatment consisted of daclatasvir-sofosbuvir with or without ribavirin and daclatasvir-simeprevir with or without ribavirin, the intention-to-treat SVR was 93%. The aforementioned results consistently demonstrated the superior treatment efficacy of DAAs for patients post-organ transplantation with HCV infection.

In this original article, Wu et al.[7] investigated the efficacy and safety of DAAs for 32 post-organ transplantation patients with chronic hepatitis C (liver: 17, kidney: 13, kidney then liver: 1, and heart: 1). They found that this difficult-to-treat group responded well to DAA treatment with favorable tolerability and safety profile. Indeed, the data from Asian patients post-organ transplantation with HCV infection are limited: a recent study[8] disclosed a 100% SVR12 in nine post-liver transplant patients receiving combined treatment with ombitasvir, paritaprevir, ritonavir, dasabuvir, and ribavirin. There were no serious adverse events except some were related to ribavirin. No graft rejection or hepatic or renal function deterioration was noticed throughout the treatment period. Furthermore, treatment efficacy and safety were comparable between patients with and without advanced liver fibrosis. Liu et al[9] had also reported a 100% SVR12 without interruption, death or serious adverse events in 12 heart transplant recipients with chronic

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HCV infection treated by sofosbuvir combined with ledipasvir or daclatasvir. Indeed, the current study is a larger cohort surveying effectiveness and safety of different regiments of DAAs for patients suffering from chronic hepatitis C following various organ transplantations in Taiwan. Since the response rate and major genotype vary among different ethnic groups and areas, the present findings are informative and have contributed more insights for this distinct patient group.

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