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Research Article

IFN-Based and IFN-Free Direct-Acting Antiviral Drug Treatments for Acquired Hepatitis C Virus in Post-Transplant Recipients

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Abstract

Background: Hepatitis C virus (HCV) re-infection occurs frequently in recipients of liver or kidney transplants (LT/KT). Interferon (IFN)-based therapies are used to treat HCV-infected individuals; however, their efficacy is low.

Methods: In total, 24 post-transplant HCV patients (12 LT and 12 KT recipients; median age, 59 years; 15 males; 21 serotype 1) were enrolled. Of these patients, eight (6 with LT) were treated with IFN-based therapy. Twenty patients received direct-acting antiviral drugs (DAAs; 12 received daclatasvir [DCV]/asunaprevir [ASV] for 24 weeks; 7 received sofosbuvir (SOF)/ledipasvir (LDV) for 12 weeks; and 1 received SOF/ribavirin for 12 weeks).

***Results*:** In two patients, HCV resolved spontaneously after LT. Only one of six patients who received IFN for ≥24 weeks, achieved sustained virological responses (SVR); three stopped treatment due to adverse events; and two relapsed. OF the LT recipients, five received DCV/ASV and four received SOF-based therapies. All nine LT patients treated with DAAs achieved SVR. Two KT patients were treated with IFN; one achieved SVR; and one discontinued IFN due to renal rejection. Of the KT patients, seven received DCV/ASV and four received SOF/LDV combinations. All 11 KT patients treated with DAAs achieved SVR. Two patients with lower estimated glomerular filtration rates (eGFR) and three patients with HCV NS5A-resistance mutations were successfully treated with DCV/ASV and SOF/LDV, respectively.

***Conclusions*:** DAAs are highly effective and safe in LT/KT recipients who have failed IFN-based therapy and have a low eGFR or the NS5A-resistance mutation.

Keywords

Liver transplantation; kidney transplantation; direct-acting antiviral drugs; tolerability; effectiveness

Introduction

The incidence of hepatitis C virus (HCV) infection among liver or kidney transplant (LT/KT) recipients is higher than that in the general population [1], and eradication of HCV is an urgent issue. HCV-related fibrosis progresses rapidly after transplantation under immunosuppressive conditions and increases the risk of mortality [2,3]. Liver fibrosis progresses in 70%–90% of patients within 1 year after undergoing LT, and develops into cirrhosis within 5 years after LT in 20% of patients [3]. Furthermore, 25%–30% of allograft losses occur in patients with HCV who have undergone LT [2,4], whereas 36%–40% of cases progress within 3–4 years after KT [5,6]. The complications of sepsis [7], new onset diabetes [8], *de novo* glomerular disease [9], and a higher risk of rejection have been reported in the KT setting.

To date, interferon (IFN)-based therapies have been the main treatment for HCV infection, even in patients who have undergone LT; however, tolerability and drug-drug interactions with calcineurin inhibitors are limiting factors for efficacy and safety [10,11]. Dose reduction and discontinued therapy are required in up to 73% and 28% of patients, respectively. Several studies using pegylated (PEG)-IFN/ribavirin (RBV) have shown sustained virological response (SVR) rates of 18%–45% after LT [12,13].

In contrast, the Kidney Disease: Improving Global Outcomes Guidelines do not recommend IFN therapy for KT recipients [14] because IFN therapy frequently induces severe rejection. Moreover, RBV should not be used in patients with creatinine clearance <50 mL/min.

HCV therapy in the transplant setting has improved dramatically due to several new combinations of direct-acting antiviral drugs (DAAs). Food and Drug Administration-approved regimens are available for genotype (GT)-1, including boceprevir/telaprevir combined with PEG-IFN/RBV, sofosbuvir (SOF)/ledipasvir (LDV), SOF/simeprevir (SMV), ritonavir (r)-boosted ombitasvir (OBV)/paritaprevir (PTV)/dasabuvir, and elbasvir/grazoprevir [15–17]. In Japan, daclatasvir (DCV)/asunaprevir (ASV) for 24 weeks, SOF/LDV for 12 weeks, OBV/PTV/r for 12 weeks, elbasvir/grazoprevir for 12 weeks, and DCV/ASV/beclabuvir for 12 weeks are approved to treat patients with GT-1 HCV, whereas SOF/RBV for 12 weeks and OBV/PTV/r +RBV for 16 weeks are currently approved for GT-2 HCV patients. Clinical trials of DAAs suggest that these regimens can achieve >80%–90% SVR rates, even in patients who have failed prior IFN-based therapy.

Thus, there has been a rapid transition from IFN-based to IFN-free DAA therapy because IFN-based therapy is poorly tolerated. However, efficacy and safety have not been comprehensively examined in transplant recipients. This study describes our experience of IFN therapy and IFN-free DAA post-transplant-acquired HCV serotype 1 or 2 in 24 HCV cases after LT and KT.

Methods

Patients and Study Design

Overall, 24 post-transplant patients (23 Japanese, 1 European) with HCV infection were enrolled in this study (12 LT and 12 KT). Six LT recipients (5 HCV serotype 1 and 1 type 2) underwent IFN-based therapy pre-transplantation; however, five did not respond, and one relapsed. No recipients received IFN therapy before KT. HCV resolved spontaneously after LT in two patients. IFN-based therapies were performed in eight patients (6 LT and 2 KT patients).

Of the LT patients, three received 24–48 weeks of PEG-IFNα-2a (Pegasys, Chugai Pharma, Tokyo, Japan [90–180 μg weekly])/weight-based RBV (Copegus, Chugai Pharma [600–1,000 mg daily]) and three patients received 24 weeks of PEG-IFNα-2a/RBV and 12 weeks of simeprevir (SMV, Sovriad [100 mg daily])/PEG-IFNα-2a/RBV. PEG-IFNα-2a, with or without RBV, was administered to two KT patients for 24–48 weeks.

The 12 patients infected with HCV serotype 1 (5 LT and 7 KT patients) received a 24-week regimen of combined NS5A and NS3 protease-targeted DAAs (DCV [Daklinza, BMS, Tokyo, Japan] 60 mg daily and ASV [Sunvepra, BMS] 200 mg daily). The seven patients infected with HCV serotype 1 (3 LT and 4 KT patients) received a 12-week regimen of NS5A protease- and NS5B polymerase-targeted DAAs (400 mg SOF/90 mg LDV [Harvoni, Gilead Sciences, Foster City, CA, USA]). One LT patient infected with HCV serotype 2 was treated with SOF (Sovardi, Gilead Sciences [400 mg daily])/weight-based RBV (Rebetol, MSD, Tokyo, Japan [800–1400 mg daily]) for 12 weeks.

L31M and Y93H mutations are associated with NS5A-resistance; the L31 and Y93 wild-type amino acids were identified by direct sequencing [18]. The NS3 mutation was not analyzed here. Laboratory data, including therapeutic drug monitoring of tacrolimus and clinical assessments, were recorded at baseline, during treatment, and at the end of treatment.

This study was conducted according to the principles of the Declaration of Helsinki and the ethical rules of the Tokyo Women's Medical University Hospital (TWMU, Tokyo, Japan). The TWMU Institutional Review Board approved the study protocol.

Follow-up and Outcomes

The patients were hospitalized and started administration of PEG-IFN/RBV ± SMV for 1–2 weeks. After discharge, the patients received PEG-IFN every week and were followed-up in terms of laboratory profiling every 2 weeks at scheduled appointments in outpatient clinics. DAAs were started orally at outpatient clinics after excluding drugs that interacted with DAAs according to pharmacists. These patients were followed-up in terms of laboratory profiling every 2 weeks, and HCV RNA was monitored every month by polymerase chain reaction TaqMan assay. SVR was defined as aviremia for more than 24 weeks after completion of antiviral therapy for HCV infection.

Statistical Analysis

The statistical analysis was performed using Student's *t*-test and the χ^2 test with JMP Pro 11 software (SAS Institute, Cary, NC, USA). A P-value < 0.05 was considered to indicate statistical significance.

Results

Characteristics of the Patients Receiving PEG-IFN/RBV and/ or DAA Therapy after LT

Twelve cirrhotic patients underwent LT. Prednisolone (PSL), tacrolimus or cyclosporine A (CyA), and mycophenolate mofetil (MMF) were prescribed as immunosuppressant therapy after transplantation. PSL was tapered gradually and discontinued on starting the HCV treatment. All patients were re-infected with HCV by the transplanted liver; however, two patients spontaneously resolved HCV within 3 months of LT. PEG-IFN/RBV ± SMV treatments were started in six cases, of which, one achieved a SVR (#LT1), one became infected with *Aspergillus* (#LT10), and two females

discontinued the treatment due to severe anemia (#LT2 and #LT3). The other two cases relapsed after withdrawal (#LT5 and #LT8). Therefore, the SVR rate of IFN-based therapy was 16.7%. DAA therapy was initiated in the remaining nine cases (8 with HCV serotype 1), including five relapsed LT cases after IFN treatment. Five cases with no NS5A-resistance mutations were treated with DCV/ASV for 24 weeks, and three cases, including one L31 mutation case, were treated with SOF/LDV for 12 weeks (Table 1).

Table 1 Baseline characteristics of LT patients who received IFN or DAA therapy for HCV infection.

Case	Age	Sex	CNI	Anti-metabolite	IFN and response	Pre-DAA	PLT	ALT	eGFR	GT	HCV RNA	DAAs	NS5A
LT1	48/-	M	TAC	MMF	Yes, SVR	(-)	30.8	65	66.0	1	7.1	(-)	
LT2	65/65	F	TAC	MMF	Yes, relapsed	SMV	19.4	23	49.1	1b	7.0	DCV/ASV	WT
LT3	61/61	F	TAC	MMF	Yes, relapsed	SMV	33.2	13	55.5	1b	7.5	DCV/ASV	WT
LT4	-/54	M	TAC	MMF	No	(-)	12.4	12	55.1	1b	6.6	DCV/ASV	WT
LT5	60/64	M	TAC	MMF	Yes, relapsed	(-)	18.4	17	51.9	1b	6.0	DCV/ASV	WT
LT6	-/66	M	TAC	MMF	No	(-)	11.7	170	38.0	1b	5.8	DCV/ASV	WT
LT7	-/60	F	TAC	MMF	No	(-)	18.2	63	81.9	1b	5.1	SOF/LDV	L31
LT8	62/63	M	TAC	MMF	Yes, relapsed	SMV	21.6	36	67.9	1a	5.8	SOF/LDV	-
LT9	-/65	F	CyA		No	(-)	17.4	65	63.2	1	7.2	SOF/LDV	
LT10	53/56	M	TAC	MMF	Yes, relapsed	(-)	20.2	15	62.9	2	6.2	SOF/RBV	-

Abbreviations: LT, liver transplantation; HCV, hepatitis C virus; IFN, interferon; CNI, calcineurin inhibitor; DAAs, direct-acting antiviral drugs; PLT, platelets ($\times 10^4/\mu L$); ALT, alanine aminotransferase (U/L); eGFR, estimated glomerular filtration rate (mL/min/1.73 m^2); GT, genotype; HCV RNA, HCV ribonucleic acid (logIU/mL); SVR, sustained virological response; F, female; M, male; TAC, tacrolimus; CyA, cyclosporine A; MMF, mycophenolate mofetil; SMV, simeprevir; DCV/ASV, daclatasvir/asunaprevir; SOF/LDV, sofosbuvir/ ledipasvir; RBV, ribavirin; NS5A, NS5A resistance mutations; WT, wild-type strain.
The data were obtained before IFN therapy in case #LT1, and before DAA therapy in cases #LT2–10. Age on receipt of IFN/DAA therapy (years). NS5A resistance mutations were not determined in #LT1 and #LT9 and not available in GT-1a and GT-2. SVR is defined as aviremia for more than 12 weeks after the completion of antiviral therapy for HCV infection.

Case #LT10, who had acquired HCV serotype 2, failed IFN-based therapy because treatment was discontinued due to an *Aspergillus* infection. He was treated with SOF/RBV for 12 weeks at 28 months after withdrawal from IFN therapy. Despite reduction in the RBV dose due to anemia, he achieved an SVR after SOF/RBV treatment.

Their eGFR was not affected during treatment and transaminase levels decreased (Figure 1a,c). No allograft rejection or dramatic adjustment in the immunosuppressant regimen occurred during the DAA treatment of the patients who underwent LT (Figure 1e). HCV RNA promptly disappeared (Figure 1g), and DAA induced an SVR lasting ≥24 weeks in all nine cases (SVR rate, 100%).

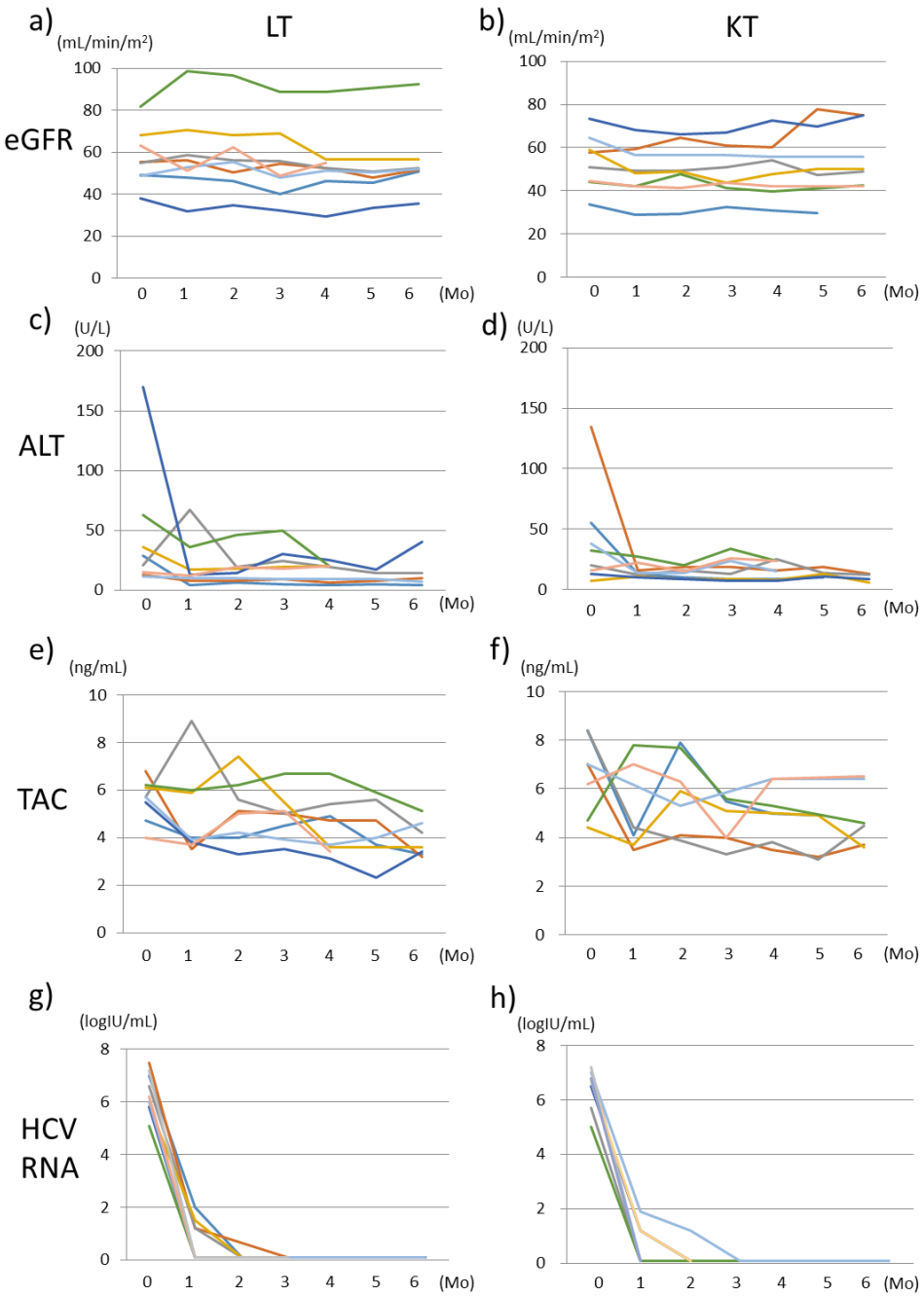

Figure 1 Changes in laboratory data during HCV treatment with DAAs. Changes in the eGFR in (a) LT and (b) KT recipients; serum ALT levels in (c) LT and (d) KT recipients; tacrolimus concentrations in (e) LT and (f) KT recipients, and HCV RNA levels in (g) LT and (h) KT recipients. The eGFR was not affected in the LT (a) or KT recipients (b) during HCV treatment. ALT levels decreased rapidly after treatment in LT (c) and KT recipients (d). Tacrolimus concentration changed slightly; however, no radical dose adjustment was required (e: LT, f: KT). No HCV RNA was detected after administering DAAs (g: LT, h: KT). Abbreviations: LT, liver transplantation; KT, kidney transplantation; eGFR, estimated glomerular filtration rate; ALT, alanine aminotransferase; TAC, tacrolimus; HCV, hepatitis C virus; Mo, months.

IFN and/or DAA Treatment in KT Recipients

Of the 12 KT recipients (Table 2), the renal disease etiology included chronic glomerulonephritis in six of these patients. None of the patients had previously used DAAs. IFN-based therapies are generally not used in KT recipients because IFN can induce severe allograft rejection. However, we treated cases #KT1 and #KT2 with PEG-IFN ± RBV.

Table 2 Baseline characteristics of KT patients who received IFN or DAA therapy to treat HCV.

Case	Age	Sex	CNI	Anti-Metabolite	Other	IFN and Response	PLT	ALT	eGFR	GT	HCV RNA	DAAs	NS5A	Renal Disease
KT1	57/-	F	TAC	MMF	MP	Yes SVR	14.5	21	24.8	2	7.3	(-)	-	MN
KT2	52/55	M	TAC	MMF	MP	Yes Relapsed	5.1	55	29.6	1b	5.8	DCV/ASV	WT	IgA
KT3	-/55	F		AZA	PSL	No	6.3	64	39.0	1b	6.7	DCV/ASV	WT	CGN
KT4	-/59	F	TAC	MMF	MP	No	11.6	32	57.6	1b	5.7	DCV/ASV	WT	CGN
KT5	-/49	M	TAC	MMF	PSL	No	13.3	20	51.1	1b	6.7	DCV/ASV	WT	Injury
KT6	-/71	M	TAC	MMF	EVE	No	11.1	16	29.6	1b	6.5	DCV/ASV	WT	CGN
KT7	-/50	M	TAC	MMF	MP	No	14.8	11	58.9	1b	7.0	DCV/ASV	WT	
KT8	-/69	M	TAC	MMF	MP	No	20.7	13	73.5	1b	5.0	DCV/ASV	WT	DM
KT9	-/67	M	TAC	MMF	MP	No	17.3	32	44.4	1b	6.8	SOF/LDV	Y93 100%	CGN
KT10	-/53	M	TAC	MMF	EVE	No	17.3	106	50.2	1	7.2	SOF/LDV		IgA
KT11	-/77	M	TAC	MMF	MP	No	12.3	38	64.4	1b	6.7	SOF/LDV	Y93 40%	CGN
KT12	-/30	M	TAC	MMF	MP	No	43.1	16	44.6	1b	6.8	SOF/LDV	WT	Renal dysplasia

Abbreviations: KT, kidney transplantation; IFN, interferon; DAAs, direct-acting antiviral drugs; HCV, hepatitis C virus; CNI, calcineurin inhibitor; PLT, platelets ($\times 10^4/\mu L$); ALT, alanine aminotransferase (U/L); eGFR, estimated glomerular filtration rate (mL/min/1.73 m^2); GT, genotype; HCV RNA, HCV ribonucleic acid (logIU/mL); SVR, sustained virological response; F, female; M, male; CGN, chronic glomerulonephritis; IgA, immunoglobulin A; DM, diabetes mellitus, TAC, tacrolimus; MMF, mycophenolate mofetil; MP, methylprednisolone; AZA, azathioprine; PSL, prednisolone; EVE, everolimus; DCV/ASV, daclatasvir/asunaprevir; SOF/LDV, sofosbuvir/ ledipasvir; NS5A, NS5A resistance mutations; WT, wild-type strain.

The data were obtained before IFN therapy in case #KT1 and from before DAA therapy in cases #KT2–12. Age on receipt of IFN/DAA therapy (years). NS5A resistance mutations were not determined in #KT10 and not available in GT-2. SVR is defined as aviremia for more than 12 weeks after the completion of antiviral therapy for HCV infection.

Case #KT1 had acquired HCV serotype 2 with suspected renal impairment due to membranous nephropathy caused by HCV. She had a low eGFR but achieved an SVR. Case #KT2 was diagnosed with fibrosing cholestatic hepatitis and was started on IFN therapy by necessity. The transaminase level improved, but the treatment was discontinued due to renal rejection. We administered DCV/ASV therapy to seven cases, including the cases of IFN failure (#KT2-8, Table 1B).

The median hemodialysis duration was 3 years (range, 0.5–26 years). Immunosuppressant therapy featured methylprednisolone (MP), PSL, or mammalian target of rapamycin (everolimus), tacrolimus, and MMF or azathioprine. Two cases had an eGFR < 30 mL/min/1.73 m^2. All seven cases possessed the L31 or Y93 wild-type strains of the NS5A polymorphisms and were treated with DCV/ASV. SVR was achieved in all cases.

Two cases, #KT9 and #KT11, had the NS5A resistance mutation and an eGFR > 30 mL/min/1.73 m^2 before receiving SOF/LDV therapy.

No severe adverse events related to renal or liver function were detected (Figure 1b,d). No allograft rejection was observed, and no immunosuppressant therapies had to be changed dramatically during DAA treatment in the KT recipients. Tacrolimus concentrations varied slightly; however, this was controlled (Figure 1f). HCV RNA was negative soon after starting DAA treatment (Figure 1h). All patients attained an SVR12, including those with the NS5A mutation (cases #KT9 and #KT11; Table 1B).

Comparison of IFN and DAA Therapies

The eGFR was not decreased after IFN-, DCV/ASV-, or SOF-based treatment (Figure 2a). The serum ALT level decreased after treatment, but no severe liver disturbance was evident in any case (Figure 2b). The concentration of tacrolimus was increased to prevent rejection in the IFN-treated cases. In contrast, the tacrolimus concentration was changed slightly in cases undergoing DCV/ASV treatment and decreased after DAA treatment was completed (Figure 2c). The HCV RNA level decreased rapidly after IFN and DAA treatment; however, it was difficult to continue IFN therapy, and a positive HCV RNA status was evident after IFN treatment (Figure 2d).

Despite obtaining an SVR after IFN-based therapy in only 16.7% of LT cases and 50.0% of KT cases, all cases achieved an SVR after DAA treatment (SVR rate, 100%) ($p < 0.05$, Figure 3). There was no difference in the efficacy of IFN and DAA treatments between LT and KT recipients. Overall, nine LT and 11 KT recipients received DAA treatment for 1.9 years (range, 0.5–20.8 years) after LT and for 5.2 years (range, 0.5–35.6 years) after KT. A negative HCV RNA status was achieved after 41 days (range, 19–123 days) of IFN treatment and 27 days (range, 12–67 days) of DAA treatment in the LT recipients and after 50 days of IFN treatment and 37 days (range, 20–85 days) of DAA treatment in the KT recipients, with no significant differences.

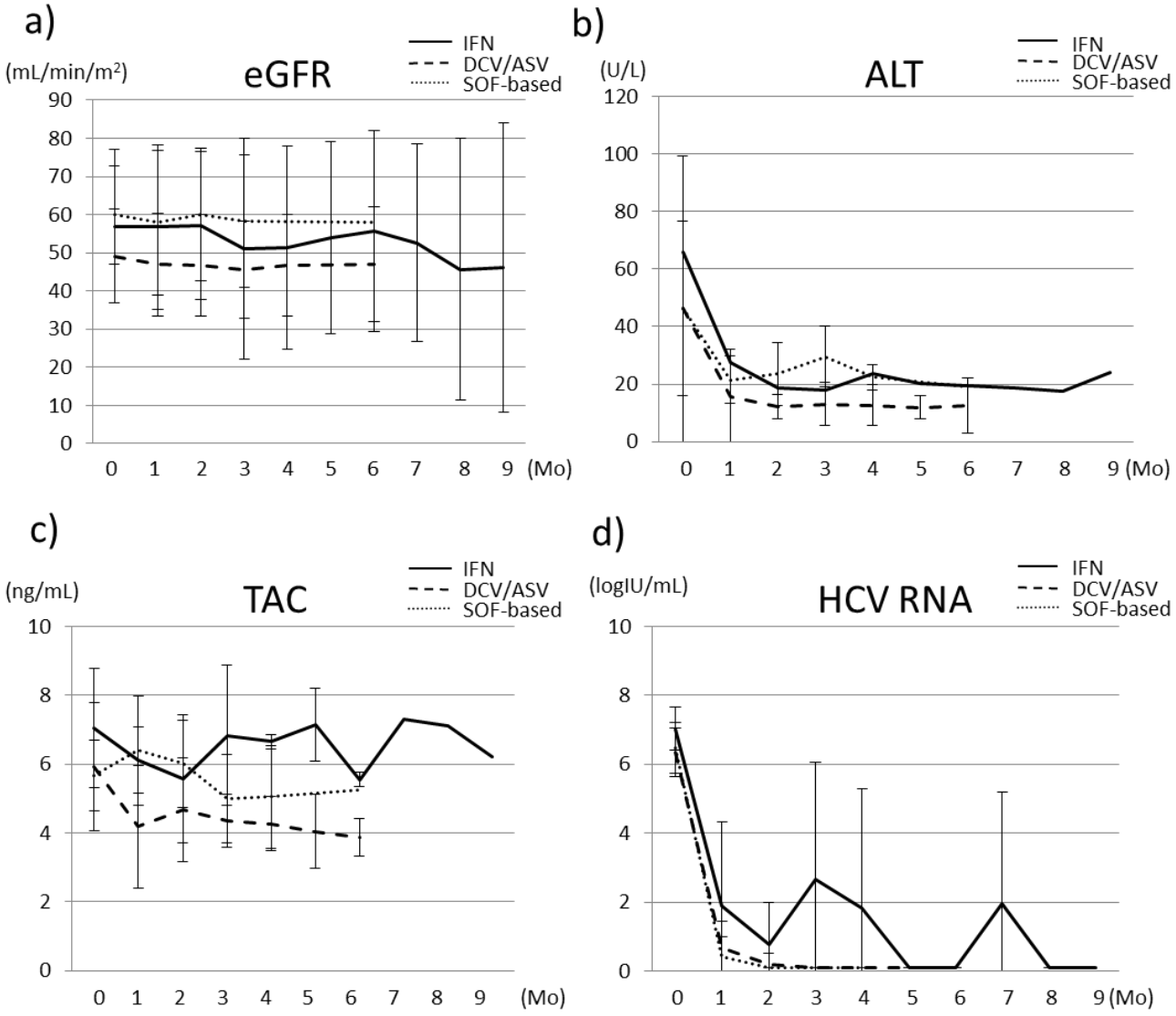

Figure 2 Changes in laboratory data during HCV treatment with IFN and DAAs. (a) eGFR, (b) ALT level, (c) tacrolimus concentration, and (d) HCV RNA level. The eGFR did not increase after IFN-, DCV/ASV-, or SOF-based treatment (a). The serum ALT level decreased after treatment, but no severe liver disturbance was noted in any of the cases (b). The concentration of tacrolimus was increased (to inhibit rejection) in the IFN-treated cases. The concentration was changed slightly after DCV/ASV treatment (c) and was reduced after completion of DAA treatment. The HCV RNA level was rapidly reduced after IFN and DAA treatment; however, it was difficult to continue IFN therapy, and a positive HCV RNA status was evident after IFN treatment (d). Abbreviations: IFN, interferon; DCV/ASV, daclatasvir/asunaprevir; SOF-based, sofosbuvir; eGFR, estimated glomerular filtration rate; ALT, alanine aminotransferase; TAC, tacrolimus; HCV, hepatitis C virus; Mo, months.

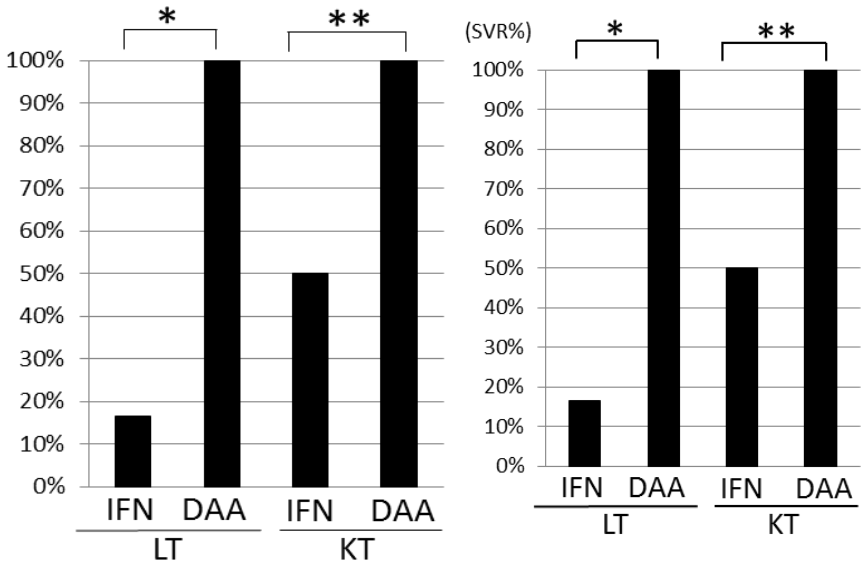

Figure 3 Comparison of SVR rates achieved by HCV treatment with IFN-based or DAA. SVR rates after IFN-based or DAA treatment. SVR rates were significantly higher in the DAA-treated cases than in those who received the IFN-based regimen both after LT and KT (*$p < 0.01$, ** $p < 0.05$ by χ^2 analysis). Abbreviations: SVR, sustained virological response HCV; hepatitis C virus; IFN, interferon; DAA, direct-acting antiviral drugs; LT, liver transplantation; KT, kidney transplantation.

Discussion

We treated 24 HCV-positive LT and KT recipients; eight cases received IFN therapy, and 20 were treated with DAAs, including six who failed to respond to IFN therapy. All patients, including those with the HCV NS5A resistance mutation or a low eGFR, achieved an SVR. No adverse events or allograft rejection were observed during DAA treatment. The DCV/ASV and SOF-based therapies were safe and effective for LT and KT recipients under immunosuppressed conditions and were superior to PEG-IFN/RBV-based therapy.

We previously reported spontaneous HCV clearance in two immunosuppressed patients receiving low-dose PSL [19]. These cases are rare in the transplant setting, and most HCV cases require treatment. PEG-IFN/RBV with or without SMV was administered to the LT recipients; however, RBV induced severe anemia due to co-administration with MMF and could not be continued, as described previously [20]. In our study, IFN therapy was discontinued due to side-effects and infection, resulting in a low SVR rate.

In general, HCV therapy is switched from IFN-based to DAA treatment to achieve higher efficacy and safety [21]. DCV/ASV was the first oral regimen for HCV GT-1b treatment approved in Japan. The efficacy of DCV/ASV is approximately 95% in patients with the wild-type strains of the GT-Ib NS5A polymorphism (L28M, L31M, and Y93H), whereas it is only effective in 40% of cases with HCV NS5A resistance mutations [22]. Thus, patients infected with wild-type NS5A strains should be selected for DCV/ASV therapy to increase efficacy. In addition, DCV/ASV therapy can be used in

patients with possible renal dysfunction, including those undergoing hemodialysis [23]. In fact, two cases with a low eGFR (<30 mL/min/1.73 m^2) who were treated with DCV/ASV did not show any deterioration in renal function.

We are the first to report the efficacy of DCV/ASV therapy in KT recipients [24]. Recent studies have demonstrated the efficacy of DAA therapies, including OBV/dasabuvir/r, SOF/LDV, and SOF/DCV, in KT recipients [25]. DAA therapy was interrupted in two patients (8%) due to hepatotoxicity and liver transplantation, with anemia related to RBV reported as a side-effect. In this study, we increased the case numbers to 12 LT and 12 KT recipients, including cases from our previous study. With reference to the wild-type NS5A GT, 12 cases were treated with DCV/ASV, and all achieved an SVR.

SOF is an inhibitor of the HCV NS5B RNA-dependent RNA polymerase and is used for HCV treatment. The guidelines of the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver make the following recommendations: (1) SOF/LDV+RBV, (2) SOF/LDV, (3) SOF/SMV with or without RBV, and 4) OBV/dasabuvir/r and RBV for 12 weeks for LT recipients [26,27]. SOF-based therapy achieved a 93.4% SVR in LT recipients, regardless of the stage of fibrosis or subtype [28,29]. In our study, we included three cases with the Y93 and L31 mutations who also achieved an SVR. Despite the high efficacy of SOF for HCV clearance, this agent is not suitable for use in patients with an eGFR <30 mL/min/1.73 m^2 or those on hemodialysis, because renal clearance is the major elimination pathway for SOF [30]. The DCV/ASV combination [31] increases the concentrations of cyclosporine and tacrolimus. Therefore, cyclosporine is contraindicated for use with DCV/ASV treatment. SOF does not interact with calcineurin inhibitors [32]. In our LT and KT recipients who received DCV/ASV and SOF/LDV or RBV therapy, the tacrolimus concentration was not affected substantially, and no allograft rejection was observed. Furthermore, we used several combinations of immunosuppressants, such as tacrolimus, cyclosporine (with SOF only), MMF, azathioprine, PSL, MP, and everolimus, and all showed tolerability to DAAs.

The efficacies of these therapies in comparison with those of IFN and DAA therapies have been reported independently. In our study, we compared efficacy in the same individual by treating with DAAs as a secondary to IFN. Overall, six patients (5 LT and 1 KT) relapsed on PEG-IFN-based therapy and were switched to DAAs, and all patients were treated successfully with DAAs (DCV/ASV, SOF/LDV, or SOF/RBV). No severe side-effects were observed in any of our cases. Therefore, our findings demonstrate the superiority of DAA treatments in terms of safety and efficacy compared the PEG-IFN-based regimen.

Conclusions

The IFN-free regimens comprising DCV/ASV, SOF/LDV, or RBV therapy were highly effective in Japanese HCV-positive LT and KT recipients receiving immunosuppressant therapy, despite the presence of the NS5A resistance mutation and pretreatment with IFN-based therapy. However, the number of subjects studied was small. Few reports exist describing the use of DAA combinations in

transplant settings, especially from Asia. We safely achieved a high SVR rate in transplant patients receiving SOF-based therapy, in those with preserved renal function. DCV/ASV was administered to patients with the wild-type NS5A HCV serotype 1 strain.

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