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Successful Sofosbuvir-Based Therapy in HIV/HCV Co-Infected Liver Transplant Recipients with Recurrent HCV Infection

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Abstract

Objective—Recurrent hepatitis C virus (HCV) infection contributes to unfavorable outcomes in HIV/HCV co-infected liver transplant (LT) recipients. Direct-acting antiviral (DAA) therapies for HCV offer an opportunity to improve patient and allograft survival in this patient population. We evaluated treatment outcomes with sofosbuvir-based DAA therapy among HIV/HCV co-infected LT recipients.

Design—Single center prospective cohort study

Methods—We identified 8 HIV/HCV co-infected LT recipients who were prospectively followed in the Northwestern University Viral Hepatitis Registry and who received sofosbuvir

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(SOF)-based DAA therapy. We evaluated responses to therapy, including sustained HCV viral response 12 weeks after therapy completion (SVR12) and adverse effects (AE).

Results—Seven recipients (87.5%) completed 12 weeks of SOF-based therapy: SOF/simeprevir for genotype 1 (n=6), SOF/ribavirin for genotype 2 (n=1). Of persons who completed therapy, all achieved SVR12. Strategies for the management of expected and observed drug interactions consequent to the addition of simeprevir to pre-existing complex medication regimens included modifications of HIV antiretroviral regimens (n=4) and tacrolimus (FK) dosing (n=4) and frequent monitoring of FK trough levels. Minor AEs were observed after DAA initiation. One episode of allograft rejection and one death occurred that were deemed unlikely related to HCV therapy.

Conclusions—High rates of HCV treatment success and no treatment-limiting AEs were observed in this HIV/HCV LT cohort. Complex drug interactions were successfully managed in the context of multidisciplinary specialty care. Further studies are needed to assess the long-term effects of DAA therapy on patient and allograft survival among HIV/HCV co-infected LT recipients.

Keywords

Human Immunodeficiency Virus; Hepatitis C Virus infection; liver transplantation; sofosbuvir; simeprevir

INTRODUCTION

Hepatitis C virus (HCV) infection is a leading cause of non-AIDS mortality in patients infected with human immunodeficiency virus (HIV) [1]. Liver transplantation (LT) is feasible for HIV/HCV co-infected patients with end stage liver disease, albeit with lower patient and graft survival rates as compared to HCV mono-infected recipients. These suboptimal outcomes are often attributed to rapidly progressive or severe recurrent HCV [2–6]. Interferon (IFN)-based regimens for post-LT treatment of HCV have low efficacy and high rates of treatment-limiting complexities, with particularly low rates of virologic cure observed in co-infected recipients [7, 8]. Emerging therapies with direct-acting antivirals (DAAs) offer promise of high rates of HCV cure, fewer side effects and improved outcomes after LT. However, no rigorous clinical trial data regarding DAAs for HCV treatment among co-infected LT recipients is available. As such, we sought to evaluate ‘real world’ treatment outcomes with DAAs among HIV/HCV co-infected LT recipients at our center.

METHODS

Study Population

The Northwestern University Viral Hepatitis Registry (NU-VHR) is a prospective cohort of HIV-infected adults co-infected with hepatitis B and/or C virus recruited at Northwestern Memorial Hospital in Chicago, Illinois since January 2013. For this analysis, we included subjects with chronic HCV infection who underwent LT between 2007 and 2014. The Institutional Review Board of NU approved this study.

Clinical and Laboratory Protocols

Per our standardized clinical protocol, HIV/HCV co-infected patients were listed for LT if they met pre-identified criteria that mirrored those established in clinical trials [6, 9]. A multi-disciplinary team provided clinical care to all recipients. All patients received combination antiretroviral therapy (cART) for HIV infection at the time of LT. Immunosuppression included methylprednisolone followed by a prednisone taper and tacrolimus (FK) with specific FK goal levels based on renal function and duration of time post-transplant; mycophenolate mofetil was added in recipients with kidney disease (Post-transplant Protocol available in Supplementary Material). Liver biopsies were performed to investigate serum liver chemistry abnormalities or at least once in the first year post-transplantation.

HCV treatment choice and duration was based on existing guidelines for HCV mono-infection [15]. HCV genotype (GT) 1 and 2 infections were treated with sofosbuvir (SOF) plus simeprevir (SMV) or ribavirin (RBV), respectively. Due to potential complex drug interactions between cART, FK, and simeprevir, a “two-step” process for implementation of DAA therapy was utilized. First cART and FK modifications were made if needed; after stabilization of FK levels, DAAs were initiated. Standard doses of SOF, SMV, and RBV were utilized. FK levels, hemoglobin and serum creatinine were monitored during therapy and patients were contacted regularly to audit medication adherence and adverse events.

Plasma hepatitis C virus RNA was quantified at baseline, end of treatment (EOT), and 12 weeks after DAA completion. Additional labs obtained at baseline and throughout therapy included FK levels, quantitative HIV RNA, CD4+ T-cell counts, liver chemistries, hemoglobin, platelet counts, creatinine and INR. APRI (aspartate transaminase-to-platelet ratio index) and FIB-4 (Fibrosis-4) scores were calculated using standard methodologies [10–13].

Data Collection

Clinical data abstracted from medical records included laboratory data as above and patient demographics, underlying liver disease, biopsy results, prior HCV treatment, co-morbid conditions, antiretroviral and immunosuppressive therapies, transplant complications and rejection episodes.

Outcomes and Statistical Analysis

The primary study outcomes were sustained HCV viral response (HCV RNA < 15 IU/mL) 12 weeks after DAA completion (SVR12) and treatment-related adverse events. Secondary outcomes were abnormalities in serum transaminase and bilirubin levels, sustained HIV viral non-suppression (HIV RNA > 20 copies/ml present on two or more consecutive samples), supra- or sub-therapeutic FK levels, and allograft rejection. Continuous variables were compared using Wilcoxon signed-rank testing and Friedman’s ANOVA (SPSS version 22.0, Armonk, NY; IBM Corp.).

RESULTS

Clinical and Transplant Characteristics of HIV/HCV Co-Infected Recipients

Of 164 liver transplants performed at our institution for HCV over the study period, nine co-infected LT recipients were evaluated for DAA therapy; one was ineligible due to renal failure. Characteristics of the eight who received DAA therapies are described in Table 1. All were male and predominantly Caucasian (57%) with median age 51 years (IQR 40.3 - 59 years). Three failed IFN-based HCV therapy; none were HCV protease inhibitor experienced. Four experienced allograft rejection at median 63.8 months (IQR 34.6 - 72.4 months) prior to DAA therapy. None had advanced fibrosis (Metavir F3) on post-LT liver biopsy performed at median 12.9 months prior to DAA initiation (range 0.9 - 57.4 months), although one had clinical hepatic decompensation with nodular regenerative hyperplasia (NRH) seen on biopsy. All received integrase-inhibitor based cART with undetectable (n=7) or minimally detectable (n=1) HIV RNA levels and median CD4 count 259 cells/mm³ (IQR 159 - 393 cells/mm³).

The median time from transplant to DAA therapy was 23.8 months (IQR 11.3 - 66.3 months). Baseline median HCV RNA was 2,212,930 IU/mL (IQR 1,314,986 - 33,577,482 IU/mL). Seven GT1 recipients were treated with 12 weeks of SOF/SMV (six GT1a, one GT1b); six completed therapy. The recipient with GT2b infection completed 12 weeks of SOF/RBV (Table 1).

DAA Treatment Response

Seven recipients completed DAA therapy and achieved SVR12; the eighth expired during therapy (see below). Decreases in transaminases, total bilirubin, APRI score and FIB-4 score occurred in six of seven patients over the course of therapy; median changes are shown in Figure 1.

Drug Modifications and Drug-Drug Interactions (DDIs)

Patients on cART containing either efavirenz (EFZ; n=3) or atazanavir/ritonavir (ATZ/r; n=1) were changed to integrase inhibitor-based regimens prior to DAA initiation to avoid drug interactions. FK doses were decreased in two patients after discontinuing EFZ and increased in the patient who discontinued ATZ/r. The patient receiving SOF/RBV underwent no cART adjustments but required first an increased then a reduced FK dose throughout DAA therapy. Additionally two patients with fluctuating kidney function during DAA therapy required tenofovir dosing adjustments. There were no significant differences in median FK levels obtained at baseline, after four weeks of therapy, and after completion of therapy (Table 1) however four patients experienced subtherapeutic FK levels during or shortly after DAA therapy. There were no toxic levels of FK and no sustained episodes of HIV virologic non-suppression during DAA therapy.

Adverse Effects of anti-HCV Therapy

Adverse effects were assessed by regular phone contact with the pharmacist and by physicians at clinical visits during DAA therapy. The frequency and severity of on-treatment

adverse effects (AEs) were minimal and are summarized in Table 1. There were no AE-related HCV DAA discontinuations.

One patient experienced allograft rejection 36 days after completing SOF/SMV in the setting of undetectable serum tacrolimus level; rejection was successfully treated with the addition of mycophenolate mofetil and pulse corticosteroids and did not affect achievement of SVR12. This patient's cART (tenofovir, emtricitabine, raltegravir) required no adjustment for DAA therapy and all seven FK levels obtained during DAA treatment were therapeutic (range 2.0 – 5.1 ng/ml). One recipient expired after 11 days of SOF/SMV therapy, eight months after LT. His post-LT course was complicated by critical illness with multisystem organ failure (MSOF) including decompensated liver disease. He had portal hypertension (hepatic venous pressure gradient = 16 mmHg), an HCV RNA of 37,508,565 IU/mL, and NRH without acute hepatitis or fibrosis seen on liver biopsy. Although not biopsy proven, early recurrent HCV infection was considered a factor in his hepatic decompensation and DAA treatment was initiated. Despite a 3-log decline in his serum HCV RNA after one week of treatment, progressive MSOF prompted the decision to withdraw care.

DISCUSSION

We herein report excellent treatment outcomes and tolerability in the largest number to date of HIV/HCV co-infected LT recipients treated with HCV DAAs, specifically SOF with SMV or RBV. Our results are comparable to, if not better than, those observed in studies of HCV mono-infected, non-transplant patients. Although no clinical trial has assessed SOF/SMV in HIV/HCV co-infected patients or LT recipients, “real world” data in HIV/HCV non-transplant patients shows this regimen to be highly effective [14, 15]. Clinical trials of other DAA combinations in mono-infected LT recipients also demonstrate high SVR12 rates; 96–98% of non-cirrhotic recipients achieved SVR12 using SOF/ledipasvir (LDV) or ombitasvir/paritaprevir/r with dasabuvir and ribavirin (3D + RBV) [16, 17]. Lower rates of virologic response were noted within non-clinical trial-based observational cohorts and among patients with advanced fibrosis or cirrhosis [18, 19].

Published studies of DAA treatment in HIV/HCV co-infected LT recipients are limited. Campos-Varela, et al. described two HIV-infected LT recipients with HCV GT 1a, one with decompensated cirrhosis and the other with severe cholestatic recurrent HCV and cirrhosis, who were treated with 24 weeks of SOF/RBV followed by 12 weeks of SOF/SMV/RBV to achieve SVR12 [20]. Our recipients, though with less advanced liver disease, were successfully treated with significantly shorter durations of HCV DAA therapy and without the addition of ribavirin for GT1-infected persons, reducing financial costs and potential adverse effects.

Though we observed minimal HCV DAA-related adverse effects and no treatment-related DAA discontinuations, frequent medication adjustments were required, emphasizing the need for intensive clinical monitoring. One patient developed acute cellular rejection after completing HCV therapy in the setting of an undetectable FK level. Simeprevir may reduce FK levels, however given the time course of this episode and documented therapeutic FK levels during and immediately after DAA therapy, it is not likely that DAAs contributed

substantively to this episode. One patient died during SOF/SMV therapy; he was critically ill at treatment initiation and supportive care was withdrawn when he failed to clinically improve. Although SMV has been associated with hepatic decompensation in patients with advanced liver disease, it was not considered a factor in this patient's clinical course [21].

This study was conducted at a single center among a small cohort, potentially limiting the generalizability of the findings. Most patients had minimal post-LT liver disease, which is not representative of HIV/HCV co-infected LT recipients with more aggressive post-LT HCV infection recurrence or advanced fibrosis. Additionally our cohort demonstrated generally excellent medication adherence and follow-up. These factors combined with intensive multi-disciplinary patient care likely contributed to our observed DAA treatment success.

In summary, our results indicate that combinations of SOF/SMV for GT1 and SOF/RBV for GT2 patients are feasible therapeutic regimens for patients with post-LT recurrent HCV and mild to moderate liver fibrosis. Longer durations or more complex regimens are not necessary solely for the reason of LT. Although DAAs with fewer drug interactions than SMV are now available, this agent is well tolerated and efficacious in non-cirrhotic patients with HCV GT1 and thus remains a treatment option for select patients [22]. In the context of limited and less than ideal LT outcomes among HIV/HCV co-infected persons, it seems prudent to target this high-risk population for prompt receipt of DAA therapy. Since HCV treatment prior to LT may be difficult or less efficacious for patients with renal failure or decompensated cirrhosis, treating such patients early after transplant is emerging as an important strategy that may significantly improve patient and graft survival.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

REFERENCES

1. Weber R, Sabin CA, Friis-Moller N, Reiss P, El-Sadr WM, Kirk O, et al. Liver-related deaths in persons infected with the human immunodeficiency virus: the D:A:D study. *Arch Intern Med.* 2006; 166:1632–1641. [PubMed: 16908797]
2. Stock PG, Terrault NA. HIV and liver transplantation: Hepatitis C is the last hurdle. *Hepatology.* 2014
3. Miro JM, Montejo M, Castells L, Rafecas A, Moreno S, Aguerro F, et al. Outcome of HCV/HIV-coinfected liver transplant recipients: a prospective and multicenter cohort study. *Am J Transplant.* 2012; 12:1866–1876. [PubMed: 22471341]
4. Duclos-Vallee JC, Feray C, Sebagh M, Teicher E, Roque-Afonso AM, Roche B, et al. Survival and recurrence of hepatitis C after liver transplantation in patients coinfecting with human immunodeficiency virus and hepatitis C virus. *Hepatology.* 2008; 47:407–417. [PubMed: 18098295]
5. de Vera ME, Dvorchik I, Tom K, Eghtesad B, Thai N, Shakil O, et al. Survival of liver transplant patients coinfecting with HIV and HCV is adversely impacted by recurrent hepatitis C. *Am J Transplant.* 2006; 6:2983–2993. [PubMed: 17062005]
6. Terrault NA, Roland ME, Schiano T, Dove L, Wong MT, Poordad F, et al. Outcomes of liver transplant recipients with hepatitis C and human immunodeficiency virus coinfection. *Liver Transpl.* 2012; 18:716–726. [PubMed: 22328294]

7. Campos-Varela I, Peters MG, Terrault NA. Advances in therapy for HIV/hepatitis C virus-coinfected patients in the liver transplant setting. *Clin Infect Dis*. 2015; 60:108–116. [PubMed: 25228702]
8. Torriani FJ, Rodriguez-Torres M, Rockstroh JK, Lissen E, Gonzalez-Garcia J, Lazzarin A, et al. Peginterferon Alfa-2a plus ribavirin for chronic hepatitis C virus infection in HIV-infected patients. *N Engl J Med*. 2004; 351:438–450. [PubMed: 15282351]
9. Roland ME, Barin B, Carlson L, Frassetto LA, Terrault NA, Hirose R, et al. HIV-infected liver and kidney transplant recipients: 1- and 3-year outcomes. *Am J Transplant*. 2008; 8:355–365. [PubMed: 18093266]
10. Pissiaia A Jr, Borderie D, Bernard D, Scatton O, Calmus Y, Conti F. APRI and FIB-4 Scores Are Useful After Liver Transplantation Independently of Etiology. *Transplant Proc*. 2009; 41:679–681. [PubMed: 19328955]
11. Toniutto P, Fabris C, Bitetto D, Falletti E, Avellini C, Rossi E, et al. Role of AST to platelet ratio index in the detection of liver fibrosis in patients with recurrent hepatitis C after liver transplantation. *J Gastroenterol Hepatol*. 2007; 22:1904–1908. [PubMed: 17914968]
12. Wai CT, Greenson JK, Fontana RJ, Kalbfleisch JD, Marrero JA, Conjeevaram HS, et al. A simple noninvasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C. *Hepatology*. 2003; 38:518–526. [PubMed: 12883497]
13. Sterling RK, Lissen E, Clumeck N, Sola R, Correa MC, Montaner J, et al. Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. *Hepatology*. 2006; 43:1317–1325. [PubMed: 16729309]
14. Del Bello, DP.; Bichoupan, K.; Yalamanchili, R.; Harty, A.; Ng, M.; Stivala, A., et al. Real-World Data on HIV positive Patients with HCV Genotype 1, 2 and 3 on Sofosbuvir- and Simeprevir-containing Regimens. Abstract 994. Program and Abstracts of the 65th Annual Meeting of the American Association for the Study of Liver Diseases; November 7-11, 2014; Boston, Massachusetts.
15. Grant, J.; Stosor, V.; Palella, F.; Green, R.; Thomas, G.; McGregor, D., et al. Successful Treatment with Direct Acting Antivirals in HIV/HCV Patients. Abstract 694. 22nd Conference on Retroviruses and Opportunistic Infections; February 23-26, 2015; Seattle, Washington.
16. Kwo PY, Mantry PS, Coakley E, Te HS, Vargas HE, Brown R Jr, et al. An interferon-free antiviral regimen for HCV after liver transplantation. *N Engl J Med*. 2014; 371:2375–2382. [PubMed: 25386767]
17. Reddy, KR.; Everson, GT.; Flamm, SL.; Denning, JM.; Arterburn, S.; Brandt-Serif, T., et al. Ledipasvir-sofosbuvir with ribavirin for the treatment of HCV in patients with post-transplant recurrence: preliminary results of a prospective, multicenter study. Abstract 8. Program and abstracts of the 65th Annual Meeting of the American Association for the Study of Liver Diseases; November 7-11, 2014; Boston, Massachusetts.
18. Brown, RS.; Reddy, K.; O'Leary, JG.; Kuo, A.; Morelli, G.; Stravitz, R., et al. Safety and Efficacy of New DAA-based Therapy for Hepatitis C Post-Transplant: Interval Results from the HCV-TARGET Longitudinal, Observational Study. Abstract LB-4. Program and Abstracts of the 65th Annual Meeting of the American Association for the Study of Liver Diseases; November 7-11, 2014; Boston, Massachusetts.
19. Pungpapong, S.; Werner, KT.; Aqel, B.; Leise, MD.; Murphy, JL.; Henry, TM., et al. Multicenter Experience using Sofosbuvir and Simeprevir with/without Ribavirin to Treat HCV Genotype 1 after Liver Transplantation. Abstract 9. Program and Abstracts of the 65th Annual Meeting of the American Association for the Study of Liver Diseases; November 7-11, 2014; Boston, Massachusetts.
20. Campos-Varela I, Straley S, Agudelo EZ, Carlson L, Terrault NA. Sofosbuvir, simeprevir, and ribavirin for the treatment of hepatitis C virus recurrence in human immunodeficiency virus/hepatitis C virus-coinfected liver transplant recipients. *Liver Transpl*. 2015; 21:272–274. [PubMed: 25332190]
21. Stine JG, Intagliata N, Shah NL, Argo CK, Caldwell SH, Lewis JH, et al. Hepatic Decompensation Likely Attributable to Simeprevir in Patients with Advanced Cirrhosis. *Dig Dis Sci*. 2014
22. Kwo, P.; Gitlin, N.; Nahas, R.; Bernstein, D.; Rojter, S.; Schiff, E., et al. A Phase 3, randomised, open-label study to evaluate the efficacy and safety of 12 and 8 weeks of simeprevir (SMV) plus

sofosbuvir (SOF) in treatment-naïve and -experienced patients with chronic HCV genotype 1 infection without cirrhosis: OPTIMIST-1. Abstract LP14. European Association for the Study of the Liver (EASL) 50th International Liver Congress (ILC); April 22-26, 2015; Vienna, Austria.

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Summary

HIV/HCV co-infected patients experience lower graft survival and higher mortality after liver transplantation than HCV mono-infected patients. Direct-acting antiviral treatment may improve outcomes though data are limited in co-infected patients. High rates of sustained viral response at week 12 post-therapy were achieved in this single-center study.

B

Figure 1. Median Change in Laboratory Parameters over Time

A: Median HCV RNA, total bilirubin (TB), APRI score and FIB-4 score at baseline, at end of direct acting antiviral (DAA) therapy (EOT) and at 12 weeks after end of therapy (SVR12). Values compared at baseline and SVR12 using Wilcoxon signed-rank test.

B: Median serum alanine transaminase (ALT) and aspartate transaminase (AST) levels at baseline, at end of direct acting antiviral (DAA) therapy (EOT) and at 12 weeks after end of therapy (SVR12). Values compared at baseline and SVR12 using Wilcoxon signed-rank test.

Table 1

Patient Characteristics and Outcomes, n=8

Characteristic/Outcome	N or median (% or IQR)
Age in years	51 (40.3–59)
Male	8 (100)
Race/Ethnicity	
Caucasian	4 (50)
African American	1 (12.5)
Hispanic	3 (37.5)
HIV/HCV risk factor ^d	
MSM	4 (50)
IVDU	3 (37.5)
Hemophilia	2 (25)
Hepatocellular carcinoma, pre-LT	3 (37.5)
Chronic kidney disease ^b	7 (87.5)
CD4+ T-cell count, cells/mm ³	259 (159–364)
HIV RNA < 50 copies/mL	8 (100)
Antiretroviral regimen at DAA initiation	
TDF + FTC + RAL	5 (62.5)
ABC + 3TC + RAL	2 (25)
ABC + 3TC + DTG	1 (12.5)
Required cART change for DAAs	4 (50)
HCV genotype	
1a	6 (75)
1b	1 (12.5)
2b	1 (12.5)
HCV RNA, log ₁₀ IU/mL	6.5 (6.3–7.4)
Fibrosis stage (METAVIR) F2	8 (100)
Months between biopsy and DAAs	12.9 ()
APRI score	0.97 (0.67–1.95)
FIB-4 score	2.42 (2.06–4.06)
Prior IFN-based HCV treatment ^c	3 (37.5)
Prior graft rejection	4 (50)
Months between rejection and DAAs	63.8 (34.6–72.4)

Characteristic/Outcome	N or median (% or IQR)
Months between LT and DAAs	23.8 (11.3–66.3)
HCV regimen	
SOF/SMV (GT1)	7 (87.5)
SOF/RBV (GT2)	1 (12.5)
Immunosuppressive regimen at DAA initiation	
FK monotherapy	5 (62.5)
FK + MMF or MPA	2 (25)
FK + prednisone	1 (12.5)
Required FK dose adjustment ^d	4 (50)
Median FK level	
Pre-DAA	4.6 (3.5–7)
After four weeks of DAA	3.8 (3.2–4.4)
Post-DAA	3.2 (2–4.2)
Adverse effects ^a	
Fatigue	2 (25)
Confusion/mental 'foginess'	2 (25)
Headache	1 (12.5)
Back pain	1 (12.5)
Peripheral edema	1 (12.5)
Low grade fever	1 (12.5)
Congestion	1 (12.5)
Post-DAA allograft rejection ^e	1 (12.5)
Death ^f	1 (12.5)
SVR12 ^g	7 (100)

Abbreviations: IQR, interquartile range; HIV, human immunodeficiency virus; HCV, hepatitis C virus; MSM, men who have sex with men; IVDU, intravenous drug use; LT, liver transplant; ABC, abacavir; 3TC, lamivudine; TDF, tenofovir; FTC, emtricitabine; RAL, raltegravir; DTG, dolutegravir; APRI, AST-to-platelet ratio index; FIB-4, fibrosis-4 score; IFN, interferon; DAA, direct acting antiviral; SOF, sofosbuvir; SMV, simeprevir; GT1, genotype 1; RBV, ribavirin; GT2, genotype 2; FK, tacrolimus; MMF, mycophenolate mofetil; MPA, mycophenolic acid; SVR12, sustained viral response at 12 weeks

^aPatients may belong to more than one category

^bGFR < 60 mL/min/1.73 m² for ≥ 3 months; no patient with GFR ≥ 30 mL/min/1.73 m²

^cNo patient received prior HCV protease inhibitor treatment or prior simeprevir/sofosbuvir therapy

^dAdjustment prior to or during DAA therapy

^ePatient experienced episode of rejection 36 days after completion of HCV therapy

^fDeath related to multi-system organ failure in patient with decompensated liver disease

^gCalculated based on 7 patients who reached 12 weeks after completion of therapy; excluding 1 death