Original Article

Increased Duration of Dual Pegylated Interferon and Ribavirin Therapy for Genotype 1 Hepatitis C Post-liver Transplantation Increases Sustained Virologic Response: A Retrospective Review

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ABSTRACT

Background/Aim: In patients with advanced post-transplant hepatitis C virus (HCV) recurrence, antiviral treatment (AVT) with interferon and ribavirin is indicated to prevent graft failure. The aim of this study was to determine and report Canadian data with respect to the safety, efficacy, and spontaneous virologic response (SVR) predictors of AVT among transplanted patients with HCV recurrence. **Patients and Methods:** A retrospective chart review was performed on patients transplanted in London, Ontario and Edmonton, Alberta from 2002 to 2012 who were treated for HCV. Demographic, medical, and treatment information was collected and analyzed. **Results:** A total of 85 patients with HCV received pegylated interferon with ribavirin post-liver transplantation and 28 of the 65 patients (43%) with genotype 1 achieved SVR. Of the patients having genotype 1 HCV who achieved SVR, there was a significantly lower stage of fibrosis (1.37 ± 0.88 vs. 1.89 ± 0.96; $P = 0.03$), increased ribavirin dose (total daily dose 1057 ± 230 vs. 856 ± 399 mg; $P = 0.02$), increased rapid virologic response (RVR) (6/27 vs. 0/31; $P = 0.05$), increased early virologic response (EVR) (28/28 vs. 18/35; $P = 0.006$), and longer duration of therapy (54.7 ± 13.4 weeks vs. 40.2 ± 18.7; $P = 0.001$). A logistic regression model using gender, age, RVR, EVR, anemia, duration of therapy, viral load, years' post-transplant, and type of organ (donation after cardiac death vs. donation after brain death) significantly predicted SVR ($P < 0.001$), with duration of therapy having a significant odds ratio of 1.078 ($P = 0.007$). **Conclusions:** This study identified factors that predict SVR in HCV-positive patients who received dual therapy post-transplantation. Extending therapy from 48 weeks to 72 weeks of dual therapy is associated with increased SVR rates. Future studies examining the role of extended therapy are needed to confirm these findings, since the current study is a retrospective one.

Key Words: Hepatitis C virus, liver transplant, retrospective study

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End stage liver disease secondary to hepatitis C virus (HCV) infection is a leading indication for liver transplantation (LT), constituting approximately 30-50% of all transplants.[1-5] HCV recurrence post-LT is universal.[3,6] Once HCV recurrence occurs, liver disease progresses at an accelerated rate. In untreated patients, acute biochemical hepatitis develops in approximately 75% of HCV recipients in the first 6 months following LT, and by the fifth postoperative year over 80% of HCV-infected liver transplant recipients will develop histologic evidence of chronic allograft injury secondary to hepatitis C, with up to 20-40% developing cirrhosis.[7,8] Nearly, 2-9% of patients with HCV recurrence will develop an aggressive cholestatic variant (i.e., fibrosing cholestatic hepatitis) that is associated with accelerated graft loss and patient death.[9,10] Overall, patients who undergo LT due to HCV have impaired patient and allograft survival compared with patients who undergo LT for other indications.[3]

HCV treatment post-LT has been fraught with disappointing results with SVR rates of dual therapy (pegylated interferon

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plus ribavirin) of around 30-40%,[8,11] compared to SVR rates of 55% in HCV-positive patients treated prior to LT.[12] Overall, treatment is poorly tolerated, with frequent need for dose reductions, especially for cytopenias, and drug discontinuation in up to 50% of patients. Optimizing drug doses is important in maximizing SVR rates. The potential factors that influence this low SVR rate includes; high proportion of patients with genotype 1 virus; high viral load at the start of treatment; high percentage of prior non-responders to therapy; side-effects that often make the use of standard doses and duration of treatment difficult; wether growth factors are used or not; and the effect of immunosuppression.[8,13] Donor characteristics such as age (<60 years) and IL28B genotype CC (rs129789860) have been shown to be predictors of SVR in patients treated with dual therapy.[10]

The present retrospective medical chart review study, comparing the factors that influence HCV-treatment SVR rates post-LT, was therefore undertaken in order to evaluate the role these factors play in determining the virologic response and clinical outcome of post-transplant HCV infections.

PATIENTS AND METHODS

This retrospective chart review was conducted at the liver transplant programs of the University of Alberta and Western University. The study protocol was reviewed and approved by the Independent Ethics Committee of each of the 2 participating centers.

Patient population

Patients who received a LT due to hepatitis C cirrhosis were eligible for the study. Only HCV positive LT recipients who received a LT from January 1, 2002 to December 31, 2011 were included. Patients underwent protocolized liver biopsies every 6 months post-LT to assess the severity of disease recurrence and to guide treatment decisions. Once stage 1-2 fibrosis was noted on liver biopsy, HCV antiviral treatment (AVT) was initiated. The standard doses of Pegylated Interferon (PEG-IFN) alpha 2a and Ribavirin were 180 mcg and 1200 mg, respectively. Due to pancytopenia, certain patients were started on dose-reduced treatment. In the Edmonton cohort, therapy was extended from 48 weeks to 72 weeks duration in patients who were slow to respond to treatment (patients with a 2 log decrease in HCV viral load at week 12 of treatment and a negative viral load at week 24 of treatment).

Of note, 29 patients (25 from London and 4 from Edmonton) had previously been included in the NOVARTIS trial (publication in preparation).

Assessments and endpoints

Data were extracted from the original patient charts and entered into a standardized spreadsheet. All collected data were de-identified and patients were assigned a unique study subject identifier.

Study data included patient demographics including age and gender, past medical history, HCV information (including genotype and viral load), medication information (including dosages and duration of therapy of ribavirin and pegylated interferon, as well as anti-rejection medications), metavir stage of liver fibrosis on liver biopsy, side-effects to anti-HCV treatment, and response to HCV treatment (early virologic response [EVR], rapid virologic response [RVR], and SVR).

The primary outcome of the study was the association between an *a priori* model to predict SVR and the proportion of patients with a SVR to the post-transplant HCV antiviral therapy. The SVR was defined as undetectable HCV-RNA serum levels at the 24-week follow-up period after cessation of the antiviral therapy. It was considered a relapse if the patient was found to have a positive viral load at any time after that 24-week period. The model included the covariates of gender, age, RVR, EVR, anemia, duration of dual therapy, viral load, years' post-LT, and use of donation after cardiac death (DCD) livers.

Secondary endpoints included exploring the association of SVR with other factors including recipient age, gender, presence of HCC, viral load, biochemical tests (creatinine and total bilirubin) duration and dosing of therapy, stage, genotype, location (Edmonton or London), organ type (DCD or donation after brain death [DBD]), RVR, EVR, use of Erythropoietin, and packed red blood cell transfusions.

Statistical analysis

Multivariate logistic regression analysis was performed on outcome measures using the covariates that were identified *a priori* as clinically relevant to the outcome. These were used to produce adjusted estimates and comparisons of the between-group difference with respect to the primary outcome. The odds ratio (OR) and 95% confidence intervals (CI) were used as estimate of the treatment effect.

Secondary outcomes included exploring the sensitivity, specificity, and likelihood ratios of the various *a priori* secondary factors to predict SVR. Average estimates are presented as means + standard deviation. No imputation or replacement of missing values was performed as all analyses were conducted on observed cases. A two-tailed $P < 0.05$ was used as the significance level in all analyses.

All statistical analyses were performed using IBM SPSS Version 20.0.0 (see http://www-01.ibm.com/support/docview.wss?uid=swg21476197; IBM Corp. Released 2012. IBM

SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.), Excel 2011 version 14.2.3 (Microsoft, Redmond, WA) and Cochrane's Revman 5.

RESULTS

Approximately, 135 total liver transplants (70 at Edmonton, Alberta, Canada and 65 at London, Ontario, Canada) and 45 liver transplants for HCV cirrhosis are performed each year. This retrospective analysis was based on the review of 85 charts of patients who underwent LT secondary to HCV cirrhosis between January 1st, 2002 and December 31st, 2011 in 2 Canadian liver transplant centers. A total of 2 patients were excluded as their genotype was unknown. 18 patients were genotype 2 or 3 (4 had genotype 2 and 14 had genotype 3). SVR was 43% (28/65) with genotype 1 and 93% (14/18) with genotype 2 and 3 ($P = 0.02$). Genotype 2 had a positive likelihood ratio (+LR) of 3.42 (95% CI 1.23-9.56), a negative likelihood ratio (−LR) of 0.74 (95% CI 0.58-0.94), and an OR of 4.63 (95% CI 1.37-15.59) for achieving SVR. With respect to anti-rejection medications, the majority of patients were taking tacrolimus (55/65) while there was less use of mycophenolate mofetil (28/65) and cyclosporine (8/65).

All further analyses were performed on the 65 patients who had genotype 1 HCV. The medical and demographic characteristics at the beginning of anti-HCV treatment are presented in Table 1. Between patients achieving SVR and not achieving SVR, a significant difference was observed in duration of therapy ($P = 0.001$), stage of fibrosis ($P = 0.03$), ribavirin dose ($P = 0.02$), RVR ($P = 0.05$) and EVR ($P = 0.006$). Age, gender, genotype (1a vs. 1b), and location (Edmonton vs. London), DCD versus non-DCD organs, PEG dose, whether they had received Erythropoietin or blood transfusions, presence of HCC, whether ribavirin required dose reduction, viral load, creatinine and total serum bilirubin, revealed no significant differences between patients achieving and not achieving SVR.

Table 2 presents the sensitivities, specificities, +LR, −LR for the *a priori* characteristics listed in Table 1. Significant factors associated with SVR were duration of therapy

Table 1: The medical and demographic characteristics at the time of beginning anti-HCV treatment post-liver transplant

	SVR			Non-SVR			Total		*P* value
	N	% SVR	% total	N	% non-SVR	% total	N	%	
Response to therapy	28		43	37		57	65	100	
Age (avg±SD)		56.43±4.72			57.33±4.34		56.94±4.49	-	0.42
Duration of treatment (avg±SD)		54.70±13.39			40.22±18.66		46.43±18.00	-	0.001
Stage (avg±SD)		1.37±0.88			1.89±0.96		1.64±0.95	-	0.03
Genotype									
1a	17	61	46	20	54	54	37	57	0.4
1b	8	29	35	15	40	65	23	35	
Location									
London	10	35	33	20	54	67	30	46	0.14
Edmonton	18	64	51	17	45	49	35	54	
Organ type									
DCD	3	10	75	1	3	25	4	6	0.22
Non-DCD	25	89	40	36	97	59	61	93	
Gender									
Men	21	75	42	29	78	58	50	76	0.75
Women	7	25	46	8	22	53	15	23	
PEG (mg, avg±SD)		169.11±49.85			148.61±43.10		157.58±46.93		0.08
Ribavirin (total daily dose, avg±SD)		1057.14±230.02			855.56±398.89		943.75±348.18		0.02
RVR	6/27	22	100	0/31	0.00	0.00	6	10.34	0.05
EVR	28/28	100	61	18/35	51.43	39.13	46	73.02	0.006
Erythropoietin	15/28	54	42	21/35	60.00	58.33	36	57.14	0.61
PRBC	16/28	57	43	21/35	60.00	56.76	37	58.73	0.82
HCC	9/22	43	53	8/31	25.81	47.06	17	32.08	0.25
Dose reduction	14/27	52	39	22/33	66.67	61.11	36	60.00	0.25
Creatinine (avg±SD)		95.26±25.89			101.31±30.18		98.68	28.33	0.41
Total Bilirubin (avg±SD)		25.41±46.15			26.91±28.62		26.25	37.07	0.88
Viral load (avg±SD)		2.20E+10±3.44E+10			1.69E+10±3.09E+10		1.88E+10±3.20E+10		0.18

SVR: Spontaneous virologic response, HCV: Hepatitis C virus, RVR: Rapid virologic response, EVR: Early virologic response, PRBC: Packed red blood cells, HCC: Hepatocellular carcinoma, DCD: Donation after cardiac death, PEG: Pegylated interferon

Table 2: Summary of diagnostic accuracy of variables in predicting HCV SVR post-LT

	Sensitivity	Specificity	+LR	−LR	OR
Age					
≤54	0.46 (0.30-0.64)	0.73 (0.57-0.85)	1.72 (0.886-3.331)	0.73 (0.49-1.09)	2.34 (0.83-6.60)
>54	0.54 (0.36-0.70)	0.27 (0.15-0.43)	0.73 (0.49-1.09)	1.72 (0.89-3.33)	0.43 (0.15-1.20)
Duration Rx					
<47	0.04 (0.01-0.18)	0.39 (0.25-0.55)	0.06 (0.01-0.42)	2.48 (1.63-3.75)	0.02 (0.00-0.20)
≥47	0.96 (0.82-0.99)	0.61 (0.45-0.75)	2.48 (1.63-3.75)	0.06 (0.01-0.42)	40.86 (4.97-335.89)
Stage					
0, 1 or 2	0.89 (0.72-0.96)	0.20 (0.10-0.36)	1.11 (0.90-1.37)	0.56 (0.16-1.95)	2.00 (0.47-8.60)
3 or 4	0.11 (0.04-0.28)	0.80 (0.64-0.90)	0.56 (0.16-2.00)	1.11 (0.90-1.37)	0.50 (0.12-2.15)
Genotype					
1a	0.68 (0.48-0.83)	0.43 (0.28-0.59)	1.19 (0.80-1.76)	0.75 (0.38-1.49)	1.59 (0.54-4.67)
1b	0.32 (0.17-0.52)	0.57 (0.41-0.72)	0.75 (0.38-1.49)	1.19 (0.80-1.76)	0.63 (0.21-1.84)
Location					
London	0.36 (0.21-0.54)	0.46 (0.31-0.62)	0.66 (0.37-1.18)	1.40 (0.90-2.18)	0.47 (0.17-1.29)
Edmonton	0.64 (0.46-0.79)	0.54 (0.38-0.69)	1.40 (0.90-2.18)	0.66 (0.37-1.18)	2.12 (0.77-5.80)
Organ type					
DCD	0.11 (0.04-0.27)	0.97 (0.86-1.00)	3.96 (0.44-36.11)	0.92 (0.80-1.06)	4.32 (0.43-43.96)
Non-DCD	0.89 (0.73-0.96)	0.03 (0.01-0.14)	0.92 (0.80-1.06)	3.96 (0.44-36.11)	0.23 (0.02-2.36)
Gender					
Men	0.75 (0.57-0.87)	0.22 (0.11-0.37)	0.96 (0.73-1.26)	1.16 (0.476-2.81)	0.83 (0.26-2.64)
Women	0.25 (0.13-0.43)	0.78 (0.63-0.89)	1.16 (0.48-2.81)	0.96 (0.73-1.26)	1.21 (0.28-3.85)
PEG (mg)					
≤150	0.29 (0.15-0.47)	0.56 (0.40-0.70)	0.64 (0.32-1.28)	1.29 (0.88-1.87)	0.5 (0.18-1.43)
>150	0.71 (0.53-0.85)	0.44 (0.30-0.60)	1.29 (0.88-1.87)	0.64 (0.32-1.28)	2.00 (0.70-5.72)
Ribavirin (total daily dose)					
<1000	0.11 (0.04-0.27)	0.56 (0.40-0.70)	0.24 (0.08-0.75)	1.61 (1.17-2.21)	0.15 (0.04-0.59)
≥1000	0.89 (0.73-0.96)	0.44 (0.30-0.60)	1.61 (1.17-2.21)	0.24 (0.08-0.75)	6.67 (1.70-26.13)
RVR					
Yes	0.22 (0.11-0.41)	1.00 (0.89-1.00)	N/A	0.78 (0.64-0.95)	N/A
No	0.78 (0.59-0.89)	0.00 (0.00-0.11)	0.78 (0.64-0.95)	N/A	N/A
EVR					
Yes	1.00 (0.88-1.00)	0.49 (0.33-0.64)	1.94 (1.4-2.68)	N/A	N/A
No	0.00 (0.00-0.12)	0.51 (0.36-0.67)	0	1.94 (1.41-2.68)	0
Erythropoietin					
Yes	0.54 (0.36-0.70)	0.40 (0.26-0.56)	0.89 (0.58-1.38)	1.16 (0.66-2.05)	0.77 (0.28-2.10)
No	0.46 (0.30-0.64)	0.60 (0.44-0.74)	1.16 (0.66-2.05)	0.89 (0.58-1.38)	1.30 (0.48-3.55)
PRBC					
Yes	0.54 (0.36-0.70)	0.40 (0.26-0.56)	0.95 (0.63-1.45)	1.07 (0.59-1.93)	0.89 (0.32-2.44)
No	0.43 (0.27-0.61)	0.60 (0.44-0.74)	1.07 (0.59-1.93)	0.95 (0.63-1.45)	1.13 (0.41-3.09)
HCC					
Yes	0.41 (0.23-0.61)	0.74 (0.57-0.86)	1.59 (0.73-3.49)	0.80 (0.531-1.19)	1.99 (0.62-6.42)
No	0.59 (0.39-0.77)	0.26 (0.14-0.43)	0.80 (0.531-1.19)	1.59 (0.73-3.49)	0.50 (0.16-1.61)
Dose reduction					
Yes	0.52 (0.34-0.69)	0.33 (0.20-0.50)	0.78 (0.50-1.20)	1.44 (0.78-2.69)	0.54 (0.19-1.53)
No	0.48 (0.31-0.66)	0.67 (0.50-0.80)	1.44 (0.78-2.69)	0.78 (0.50-1.20)	1.86 (0.65-5.29)
Creatinine					
<100	0.70 (0.52-0.84)	0.46 (0.30-0.62)	1.30 (0.88-1.92)	0.65 (0.33-1.29)	2.00 (0.69-5.78)
≥100	0.30 (0.16-0.48)	0.54 (0.38-0.70)	0.65 (0.33-1.29)	1.30 (0.88-1.92)	0.50 (0.17-1.44)
Total Bilirubin					
<25	0.89 (0.72-0.96)	0.32 (0.19-0.49)	1.31 (1.01-1.72)	0.34 (0.11-1.11)	3.83 (0.95-15.50)
≥25	0.11 (0.04-0.28)	0.68 (0.51-0.81)	0.34 (0.11-1.11)	1.31 (1.01-1.72)	0.26 (0.07-1.06)
Viral load					
<1E+7	0.40 (0.22-0.61)	0.41 (0.26-0.58)	0.68 (0.37-1.25)	1.46 (0.85-2.50)	0.47 (0.15-1.44)

contd...

Table 2: Contd...

	Sensitivity	Specificity	+LR	−LR	OR
>1E+7	0.60 (0.39-0.78)	0.59 (0.42-0.74)	1.46 (0.85-2.50)	0.68 (0.37-1.25)	2.14 (0.70-6.60)

HCV: Hepatitis C virus, SVR: Spontaneous virologic response, LI: Liver transplantation, RVR: Rapid virologic response, EVR: Early virologic response, LR: Likelihood ratio, OR: Odds ratio, PRBC: Packed red blood cells, HCC: Hepatocellular carcinoma, DCD: Donation after cardiac death, PEG: Pegylated interferon

Table 3: Side effects during dual HCV treatment post liver transplantation

	SVR			Non SVR			Total		*P* value
	N	% SVR	% total	*N*	% non-SVR	% total	Number	%	
Total side effects	25	89	41	36	97	59	61	94	0.13
Anemia	17	61	43	23	62	58	40	62	0.91
Leukopenia	25	89	45	30	81	55	55	85	0.37
Thrombocytopenia	1	4	13	7	19	88	8	12	0.09
Hypertension		0	0	3	8	100	3	5	0.25
Hepatitis		0	0	1	3	100	1	2	0.61
Major depression		0	0	1	3	100	1	2	0.61
Gastrointestinal bleeding		0	0	1	3	100	1	2	0.61
No side-effects	3	11	75	1	3	25	4	6	0.22
Total patients	28	100	43	37	100	57	65	100	

HCV: Hepatitis C virus, SVR: Spontaneous virologic response

48 weeks or more (+LR 2.48, CI 1.63-3.75 and –LR 0.06, CI 0.01-0.42), ribavirin dose of 1000 mg or more (+LR 1.61, CI 1.17-2.21 and –LR 0.24, CI 0.08-0.75), and presence of RVR (−LR 0.78, CI 0.64-0.95), presence of EVR (+LR 1.94, CI 1.4-2.68).

Logistic regression using gender, age, RVR, EVR, anemia, duration of therapy, viral load, years' post-transplant, and type of organ (DCD vs. DBD) to predict SVR was significant ($P < 0.001$). Duration of therapy had the only significant OR of 1.078 (i.e., for every extra week of therapy, SVR increased 1.078 times; $P = 0.007$).

Table 3 shows the number of patients who experienced side-effects while receiving anti-HCV treatment. There was no significant difference between the rates of any specific side-effects or total side-effects between patients who achieved SVR and those who did not.

DISCUSSION

The present retrospective study consisted of a Canadian cohort of patients who underwent LT for HCV-related cirrhosis and subsequently treated with dual therapy for recurrence of their HCV. It attempted to determine the factors that influence SVR rates.

Our SVR results were generally in agreement with those obtained in other post-transplant studies, although there were some differences. The SVR rate seen in this study was significantly lower for genotype 1 (43%) than for genotypes 2/3 (93%, $P = 0.02$). This is consistent with other trials. Selzner *et al.*,[14] demonstrated an overall SVR rate of 50% (genotype 1/4:40%; genotype 2/3:76%). In the trial by Cescon *et al.*,[15] the overall SVR rate was 25% (25/99), with logistic regression demonstrating that a viral genotype other than 1 significantly predicted SVR (OR = 4.97, 95% CI = 1.59-15.48, $P = 0.006$).

Previous studies have investigated the characteristics that may be important in determining SVR post-LT. The ReVIS-TC Study[16] found that the administration of cyclosporine A (CsA) (OR 0.37, $P = 0.021$) in conjunction with a longer AVT duration (OR 0.86, $P = 0.024$) correlated with lower relapse rate, whereas, the older age of the donor (OR 1.03, $P = 0.006$) and the presence of genotype 1 (OR 3.45, $P = 0.032$) were associated with a higher probability of relapse. Selzner *et al.*,[14] found SVR was higher on CsA (56%) than on tacrolimus (44%, $P = 0.05$), largely because of a lower relapse rate (6% vs. 19%, $P = 0.01$). In multivariate analysis, genotype 2/3, CsA use, donor age, and pre-treatment necroinflammatory activity were independently associated with SVR. SVR significantly improved the histology and long-term survival (actuarial 5-year survival 96% vs. 69% in non-responders, $P < 0.0001$). Cescon *et al.*,[15] demonstrated, using the logistic regression analysis, that donor age < 60 years (OR = 4.45, 95% CI = 1.39-14.19, $P = 0.01$), viral genotype other than 1 (OR = 4.97, 95% CI = 1.59-15.48, $P = 0.006$), and the use of CyA during treatment (OR = 6.85, 95% CI = 2.15-21.73, $P = 0.001$). CsA was reported to be clinically effective against HCV.[17] Controlled trials showed that a combination of CsA with IFN alpha is more effective than IFN alpha alone, especially in patients with a high viral load.[18,19] Moreover, recent *in vitro*

studies provided evidence that CsA prevents both HCV RNA replication and HCV protein production in an IFN alpha-independent manner.[20-24] Other potential predictors of SVR with dual therapy in patients pre-LT include recipient factors (non-genotype 1, IL28B genotype CC (rs129789860), low pre-treatment viral load, mild histologic disease, lower body weight, male gender, and immunosuppression with cyclosporine), donor characteristics (donor age less than 60, and IL28B genotype CC rs129789860), and treatment factors (RVR, EVR, absence of drug interactions or reductions, and use of growth factors).[10]

Strengths of our study would include 100% patient follow-up and this being a dual-centred study, which captures two large provincial LT centers, making the findings more generalizable.

This study has limitations. It is a retrospective study with a relatively small sample size. This current study did not collect information on donor age, which has been previously shown to be a major determinant of fibrosis progression.[25,26] We also did not perform an analysis on the effect of anti-rejection medications on HCV SVR rates post-LT, as there was a significant amount of evidence on the topic.[14-16] We also failed to investigate IL28 status in both donors and recipients as this may have shed light on the SVR rates. The patients undergoing HCV treatment post-LT are highly selected, and this may in part explain differences in SVR rates amongst the published studies.

Another limitation is that this study did not assess the use of triple therapy for HCV post-LT. While use of protease inhibitors (telaprevir and boceprevir) is currently not the standard of care in treating recurrent HCV in patients having undergone LT, there is great hope that they will improve the results of pre- and post-transplant antiviral therapy and become standard of care in the future. Nevertheless, the adverse profile of triple therapy in this population is still unknown and the patients that should receive it remain undefined. However, for several reasons, there is still value in this study. The first is that, at the present time, there has only been one peer-reviewed publication in 9 patients on the use of protease inhibitors in post-transplant hepatitis,[27] albeit many more forthcoming. There are also concerns of interactions between the protease inhibitors and immunosuppressant medications used to prevent hepatic rejection. Thirdly, many patients will not have access to triple therapy in the foreseeable future.

In conclusion, our study has shown that a longer duration of treatment may be associated with a higher rate of sustained viral response in the treatment of post-liver transplant patients with HCV recurrence. In addition to the duration of therapy, we identified stage of fibrosis, ribavirin dose, RVR and EVR as predictors of SVR. Given the retrospective nature of this study, further prospective longitudinal studies should be undertaken to better assess these factors, especially as they relate to triple therapy, in liver transplant recipients with HCV recurrence.

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