Tolerability and effectiveness of sofosbuvir and simeprevir in the post-transplant setting: systematic review and meta-analysis

Nghia H Nguyen,¹ Brittany E Yee,¹ Christine Chang,² Minjuan Jin,³ Glen Lutchman,² Joseph K Lim,⁴ Mindie H Nguyen,²

To cite: Nguyen NH, Yee BE, Chang C, *et al.* Tolerability and effectiveness of sofosbuvir and simeprevir in the post-transplant setting: systematic review and meta-analysis. *BMJ Open Gastro* 2016;**3**:e000066. doi:10.1136/bmjgast-2015-000066

Received 19 October 2015
Revised 18 November 2015
Accepted 20 November 2015

ABSTRACT

Background: Outcome data on simeprevir and sofosbuvir (SMV+SOF) in patients with liver transplantation (LT) with hepatitis C virus genotype 1 (HCV-1) are limited with individual studies having a small sample size and limited SVR12 (sustained virological response) data. Our goal was to perform a meta-analysis to study the outcome of SMV+SOF ±ribavirin (RBV) in recipients with LT.

Methods: In April 2015, we conducted a literature search for 'simeprevir' in MEDLINE/EMBASE and five major liver meetings. We included studies with SVR12 data in ≥5 post-LT mono-infected HCV-1 patients treated with SMV+SOF±RBV. We used random-effects models to estimate effect sizes, and the Cochrane Q-test (p value <0.10) with I² (>50%) to assess study heterogeneity.

Results: We included nine studies with a total of 325 patients with post-LT. Studies included mostly men (59–81%). Pooled SVR12 was 88.0% (95% CI 83.4% to 91.5%). In two studies, HCV-1a patients with mild fibrosis (n=108) had an SVR12 rate of 95.0% (95% CI 82.4% to 98.7%), which was significantly higher than that of HCV-1a patients with advanced fibrosis (n=49) with an SVR12 rate of 81.7% (95% CI 69.8% to 89.5%), OR 4.2 (95% CI 1.1 to 16.1, p=0.03). The most common pooled side effects were: fatigue 21% (n=48/237), headache 9% (n=23/254), dermatological symptoms 15% (n=38/254), and gastrointestinal symptoms 6% (12/193).

Conclusions: SMV+SOF±RBV is safe and effective in recipients with LT with HCV-1 infection.

INTRODUCTION

In the USA, approximately 5000 liver transplantations are performed annually with HCV accounting for approximately 40% of all cases.¹ While liver transplantation is a curative treatment for end-stage-liver-disease (ESLD), HCV recurrence after transplantation is universal in patients who are viraemic prior to transplantation.^{2,3} Furthermore, when patients receive immunosuppressive therapy in the post-transplant setting, HCV viraemia may increase and accelerate fibrosis

progression. Thus, a significant proportion of recipients with LT (20–30%) progress to cirrhosis within 5 years after transplantation.²

Historically, HCV recurrence with genotype 1 has been treated with interferon-based therapies but is associated with poor sustained virological response (SVR) rates (13–43%) and high incidence of treatment-limiting adverse events.⁴ Additionally, these trends are even more abysmal in patients with advanced fibrosis who tend to be sicker and more vulnerable to significant treatment side effects.⁵ With the recent introduction of first-generation NS3/4 protease inhibitor (PI)-based therapies, SVR rates have greatly improved with up to 60% of patients achieving SVR in this setting;^{6,7} however, owing to drug–drug interactions with calcineurin inhibitors and significant adverse events (SAEs), the adoption of these therapies in the post-LT setting has been limited.^{6–9}

Recently, all-oral regimens, including simeprevir and sofosbuvir (SMV+SOF), became available for the treatment of patients with pre-transplant with hepatitis C virus genotype 1 (HCV GT1). In the COSMOS study, this regimen demonstrated >95% SVR and had excellent tolerability.¹⁰ While this regimen is an exciting option for the treatment of HCV, there are currently limited treatment and tolerability data of SMV+SOF in the post-transplant setting.

Owing to the limited treatment options in the post-LT setting and sparse published results on SMV+SOF, our goal was to perform a meta-analysis of the available data to estimate pooled SVR rates for SMV+SOF ±ribavirin (RBV) in patients with post-LT.

MATERIALS AND METHODS

Data sources and searches

In April 2015, we comprehensively reviewed the literature by performing the search term, 'simeprevir', in the MEDLINE and EMBASE databases and included studies in

For numbered affiliations see end of article.

Correspondence to

Dr Mindie H Nguyen;
mindiehn@stanford.edu

non-English languages. During the review process, we restricted our search to studies with SMV+SOF. We also used the same search term to manually review all abstracts from five major international meetings held during 2014: the American Association for the Study of Liver Disease (AASLD), the Asian Pacific Study of the Liver (APASL), the Digestive Disease Week (DDW), the European Association for the Study of the Liver (EASL) and the World Transplant Congress.

Study selection

Our inclusion criteria were studies with ≥ 5 post-LT HCV-1 patients treated with SMV+SOF $\pm$ RBV that had SVR12 data. Our exclusion criteria were studies with patient cohorts which were co-infected with hepatitis B, hepatitis D or HIV. Articles were reviewed independently by two authors (NHN and BEY) and validated by a third (MHN), with discrepancies resolved by a consensus decision.

Data extraction

We used a case report form to collect information on study characteristics (country of origin, practice setting and collaboration), intention-to-treat analysis (ITT), study design (retrospective vs prospective) and baseline patient characteristics, which included ethnicity, age, gender, fibrosis and HCV RNA levels. We also collected baseline treatment information, treatment response (end of treatment response defined as undetectable HCV RNA at the end of treatment) and SVR.

Statistical analyses

Effect sizes were collected as pooled event rates (SVR12) with corresponding 95% CIs using random-effects models and the inverse variance method. For subgroup analyses, we used ORs and corresponding 95% CIs. We used the χ^2 -based Cochrane Q-statistic with $p \leq 0.10$ and $I^2 \geq 50\%$ as measures of substantial study heterogeneity in our models. All statistical tests were two sided, with a p value < 0.05 considered to be statistically significant. All statistical analyses were performed using Comprehensive Meta-Analysis, V.2 (Biostat, Englewood, New Jersey, USA).

RESULTS

Study search results

We identified a total of 930 articles and abstracts from MEDLINE/EMBASE and 54 abstracts from AASLD, DDW, APASL, EASL and the World Transplant Congress. We removed 182 duplicates and then screened the remaining 802 studies. We identified 39 studies that were assessed for eligibility, of which 30 were removed for various reasons (figure 1). Ultimately, seven abstracts and two full-length articles were included in the qualitative and quantitative analysis.^{11–19} The characteristics of these nine studies are described in table 1.

Study and patient characteristics

The primary analysis included 325 recipients with LT with SVR12 data (table 1). The majority were single-centre studies ($n=8$).^{11 12 14–19} All were performed in the USA and included patients with post-LT treated with SMV+SOF $\pm$ RBV for 12 weeks.^{11–19} Two studies directly compared patients with GT1a and stratified by mild versus advanced fibrosis.^{13 16} Most patients were Caucasian, had HCV-1a, male, with a mean age of approximately 60 years, and received tacrolimus as part of their immunosuppression (table 1).

SVR12 in patients with post-LT treated with SMV+SOF $\pm$ RBV

The pooled rate of SVR12 was 88% (95% CI 83.4% to 91.5%) (Q-statistic=8.70, $p=0.37$; $I^2=8.06\%$) in 325 patients with post-LT (figure 2). There was no difference ($p=0.60$) in SVR12 rates when comparing studies of a prospective, 88.9% (95% CI 83.5% to 92.6%), versus retrospective, 86.5% (95% CI 76.1% to 92.7%), study design, ($p=0.60$).

Two studies provided SVR12 and fibrosis data on a total of 108 HCV-1a patients with mild fibrosis and 49 HCV-1a patients with advanced fibrosis.^{13 16} Advanced fibrosis was defined as METAVIR F3–F4. There was a trend for a higher SVR12 rate, 93.6% (95% CI 86.8% to 97.0%), in patients with mild fibrosis than in patients with advanced fibrosis, 76.9% (95% CI 62.3% to 87.1%), OR 5.4 (95% CI 0.87 to 33.13; $p=0.069$) (figure 3).

While some studies reported the use of RBV in combination with SMV+SOF, data were not available for pooled analyses and comparison of SMV+SOF versus SMV+SOF+RBV.

Tolerability of SMV+SOF $\pm$ RBV

In studies with available tolerability data, the most common pooled side effects were: fatigue 21% ($n=48/237$), skin symptoms (which included rash, pruritus or photosensitivity) 15% ($n=38/254$), headache 9% ($n=23/254$), and GI symptoms (which included nausea or diarrhoea) 6% ($n=12/193$) (table 2). Data were not available to evaluate the incidence of anaemia in those who received RBV versus those who did not. While data were not available for pooled analysis, the majority of the studies did not report any significant dose reductions, withdrawals secondary to side effects of treatment, or interruption of immunosuppressive therapy.

DISCUSSION

In the post-LT setting, interferon-based regimens are associated with low rates of virological response and high rates of treatment-limiting adverse events.^{4 7–9 20} Among recipients with LT with HCV, viral recurrence is universal and associated with a high risk of graft loss and re-transplantation.^{1 3} Therefore, there is a need for more effective, better tolerated regimens for patients with post-transplant HCV infection. Given the promising treatment data in patients with non-transplantation from

Figure 1 PRISMA flow diagram of included studies (SVR, sustained virological response).

the COSMOS study, SOF+SMV may offer an attractive alternative in the post-LT setting.¹⁰

In the current meta-analysis, we included nine studies with a total of 325 patients with post-LT who had recurrent HCV GT1 treated with SMV+SOF±RBV. The pooled rate of SVR12 was 88.0% (95% CI 83.4% to 91.5%), which is modestly lower than SVR12 rates in patients with non-LT in the COSMOS study treated with SMV+SOF±RBV (90–94%).¹⁰ The rates were not significantly different between studies that retrospectively enrolled patients compared to those with prospective enrolment, which may reflect the lower discontinuation rates with all oral regimens compared to older interferon-based regimens. Data from the HCV-TARGET network were not included in our study because our primary objective at the time of data collection was to obtain SVR12 data but only SVR4 data were presented at the time. Additionally, data from the recently published article by Saab *et al.*²¹ were not included, since results from this study were also not available for data collection at the time; however, the SVR rate in this study was 93%, which is similar to our pooled SVR estimate.

In the two studies with available SVR12 and fibrosis data, we observed a trend for a higher SVR12 rate in HCV-1a patients with mild fibrosis, 93.6%, compared to

those with advanced fibrosis, 76.9%. The SVR12 result in patients with mild fibrosis was similar to that in cohort 1 (patients with METAVIR F0-F2) of the COSMOS study, while the rate in the advanced fibrosis group was lower than that in Cohort 2 (patients with METAVIR F3-F4) from the same study, which suggests that SMV SOF is not as effective in recipients with LT with advanced fibrosis.¹⁰

In terms of safety and tolerability, the most commonly identified side effects were fatigue 21% (n=48/237), skin problems 15% (n=38/254), and headache 9% (n=23/254). None of the individual studies reported any significant dose reductions, discontinuations in immunosuppression therapy (which consisted mostly of tacrolimus) and/or treatment discontinuations. In the study by Pungpapong *et al.*,¹³ approximately 72% of the 25 patients who received RBV developed anaemia that required dose reduction or an intervention. However, additional data from other studies to evaluate the effectiveness and safety of adding RBV versus not adding RBV were not available.

While a majority of studies have yet to be completed and there may be non-significant and significant adverse events to report, the current data from our study suggest that SMV+SOF±RBV is a safe and efficacious treatment

Table 1 Study characteristics*

First author, year	Collaboration	Sample size with SVR12 data	Proportion of genotype 1a (%)	In combination with ribavirin†	Age (years)	Male, N (%)	Advanced fibrosis, N (%)	Median or mean time to post-LT treatment in months or years	Proportion with tacrolimus use (%)
Pungpapong, 2015 ¹³	Multicentre	105	60	Mix	61.6±6	77 (76)	37 (37)	32 (2–317) months	91
Gutierrez, 2015 ¹⁶	Single centre	61	57	Without	60.2±9.3	22 (59)	14 (38)	5.4 years (1.9–8.4)	80
Gordon, 2014 ¹⁷	Single centre	15	–	Without	–	–	1 (6)	–	82
Suliman, 2014 ¹¹	Single centre	8	90	Without	62.5	6 (60)	–	–	–
Lutchman, 2014 ¹⁵	Single centre	31	64	Without	61.2±7.1	43 (81)	11 (33)	47.0 (1.4–1278.3) months	96
Nair, 2014 ¹⁴	Single centre	27	70	With	56±5	28 (61)	19 (41)	0.9±1.6 years	78
Ripper, 2014 ¹²	Single centre	23	60	Mix	60.9	21 (84)	7 (28)	32.3 (2–215.2) months	76
Crittenden, 2014 ¹⁹	Single centre	18	74	Mix	–	–	–	–	–
Ford, 2014 ¹⁸	Single centre	37	68	Mix	57	27 (73)	8 (22)	–	62

*Proportions and mean±SD were provided/abstracted from the total number of patients available from each study.

†Classification of studies that included patients: with ribavirin, without ribavirin, or a mix of patients with and without ribavirin.

LT, liver transplantation; SVR, sustained virological response.

Figure 2 Pooled rate of SVR12 in patients treated with SMV+SOF ±RBV (RBV, ribavirin; SOF, sofosbuvir; SVR, sustained virological response; SMV, simeprevir).

Overall SVR12

option compared to the older and more recent PI-based therapies.^{4 6 20} The improved simplicity and tolerability of this regimen would be expected to enhance patient adherence, increase treatment completion and optimise SVR in real-world settings.^{4 6 20}

With the recent introduction of newer and more potent direct-acting agents (DAAs) against HCV, there have been additional new combinations of anti-HCV medications that have given clinicians many more choices in the post-LT setting.²² In a phase 2 clinical trial with 40 patients (33 patients with genotype 1 and 7 patients with non-genotype 1) treated with SOF+RBV for 24 weeks, Charlton *et al*²³ observed that 67% (n=22/33) of genotype 1 patients achieved SVR12. In a different phase 2 study of 34 genotype 1 patients treated with an all-oral combination of ABT-450/r/ombitasvir, dasabuvir and RBV for 24 weeks, Mantry *et al* observed an SVR12 rate of 97%.²² The study included 223 patients (221 with genotype 1) who have started treatment and preliminary SVR12 result showed that 93% of the entire cohort achieved SVR12 (n=199/214; 9 patients have yet to reach week 12 post-treatment visit).²² Recently, a study by Charlton *et al*²⁴ on ledipasvir+SOF for the treatment of HCV in patients with pre-transplantation and post-transplantation has shown that a high SVR rate can be achieved in patients with post-LT treated for 12 weeks: 96% (n=53/55) in patients without cirrhosis, 96% (n=25/26) in patients with cirrhosis Child-Pugh Class A, 85% (n=22/26) in patients with cirrhosis Child-Pugh Class B, 60% (n=3/5) in patients with cirrhosis Child-Pugh Class C, and 100% (n=4/4) with fibrosing cholestatic hepatitis. While the final results of the studies on SMV+SOF have yet to be completed and

published, the results from our current study in a large, diverse patient population in real-world settings can provide clinicians with helpful information on an effective and tolerable treatment option.

Given the different combinations and similar treatment efficacies among the new DAAs, cost becomes an important determinant. Recent base-case analyses of the latest oral regimens compared to previous triple therapy (boceprevir–RBV–pegylated interferon) in patients with genotype 1 non-LT help to provide cost estimates that allow clinicians to make cost-conscious options.²⁵ Estimates assume that SOF, SMV, daclatasvir and ledipasvir cost \$7000, \$5500, \$5500 and \$875 per week, respectively, with results from this study suggesting that SOF-ledipasvir is the most cost-effective for genotype 1 and costs \$12 825 more per quality-adjusted life compared to previous triple therapy.²⁵ However, results from these studies are based on clinical trials and in patients with pre-LT, so additional studies are needed to confirm the cost-effectiveness of this combination when directly compared to SMV+SOF and other SOF-based therapies in the treatment of patients with non-LT.

One of the limitations of our meta-analysis was the small number of studies available, which affected our ability to detect significant publication bias. We also used random-effects models to provide a more conservative estimate for all our analyses. Although most of our data were from observational studies, our findings are more likely to be generalisable to patients in routine clinical settings, since observational studies have broader inclusion criteria for study patients. Furthermore, additional information on SMV+SOF±RBV in the future will

Figure 3 Pooled rate of SVR12 in HCV-1a patients stratified by fibrosis (mild vs advanced) (HCV, hepatitis C virus; SVR, sustained virological response).

Odds of SVR12 in Mild vs Advanced Fibrosis – HCV1a only

Table 2 Pooled side effects*

Side effects	Pungpapong <i>et al.</i> ¹³ n/N (%)	Gutierrez <i>et al.</i> ¹⁶ n/N (%)	Lutchman <i>et al.</i> ¹⁵ n/N (%)	Gordon <i>et al.</i> ¹⁷ n/N (%)	Pooled total, n/N (%)
Fatigue	16/123 (13)	17/61 (28)	15/53 (28)	–	48/237 (21)
Skin problems (rash, pruritus or photosensitivity)	7/123 (6)	7/61 (11)	22/53 (42)	2/17 (12)	38/254 (15)
Headache	6/123 (5)	11/61 (18)	4/53 (8)	2/17 (12)	23/254 (9%)
GI symptoms (nausea or diarrhoea)	6/123 (5)	–	2/53 (4)	4/17 (24)	12/193 (6)
Dyspnoea	5/123 (4)	–	–	–	
Insomnia	2/123 (2)	–	10/53 (19)	–	

*Proportions reported in all patients for each study with available side effect data.
GI, gastrointestinal.

mostly be from phase III and IV trials that are currently underway in patients with non-transplantation.^{26–28}

While there is currently one ongoing phase II trial in recipients with LT (sponsored by Janssen Scientific Affairs, LLC), the planned enrolment is only for 45 patients and data from this cohort will not be available in the immediate future.²⁹ Lastly, while there are now new data to suggest that 24 weeks of duration is better for patients with post-LT with advanced fibrosis compared to 12 weeks, the data that were available at the time of our analysis did not allow us to compare the treatment effectiveness of SMV+SOF in patients with advanced fibrosis treated for 12 vs 24 weeks.³⁰ Therefore, given the need for improved therapy in the treatment of HCV in the post-transplant setting, the current meta-analysis provides practitioners with a reasonable estimate of SVR that can be expected with SMV+SOV±RBV in this patient population.

In summary, our meta-analysis represents the first systematic review to report SVR12 data in the post-LT setting for a total of 325 patients from nine individual studies. Data from the current analysis suggest that SMV+SOV±RBV is a highly effective treatment with an SVR rate (88%) and excellent tolerability compared to prior historical therapies. Although limited by the sample size, early data in patients with advanced fibrosis indicate that this treatment option may produce a high probability of cure in similar patients. Given the interim nature of the data, additional studies with SVR12 data are needed to corroborate the findings in our study.

Author affiliations

¹School of Medicine, University of California, San Diego, La Jolla, California, USA

²Department of Gastroenterology and Hepatology, Stanford University Medical Center, Palo Alto, California, USA

³Department of Epidemiology and Biostatistics, Zhejiang University School of Public Health, Hang Zhou, China

⁴Yale Liver Center, Yale University School of Medicine, New Haven, Connecticut, USA

Contributors NHN contributed to study design, data collection, data analysis and interpretation, drafting of the manuscript. BEY contributed to data collection, data analysis and interpretation, and participation in the drafting of the manuscript. CC contributed to data collection, data analysis and

interpretation, and critical review of the manuscript. MJ contributed to data analysis and interpretation and critical revision of the manuscript. GL contributed to critical review of the manuscript. JKL contributed to data interpretation and critical revision of the manuscript. MHN contributed to concept development, study design, data collection, data analysis and interpretation, and critical revision of the manuscript. All authors identified above have critically reviewed the paper and approve the final version of this paper, including the authorship statement. MHN is the guarantor.

Competing interests GL has served as a consultant and as an advisory board member for Gilead Sciences, Janssen and Abbvie. JKL has received research support from Abbott, Boehringer-Ingelheim, Bristol-Myers Squibb, Gilead, Glaxo-Smith Kline and Janssen, and has served as a consultant and/or advisory board member for Bristol-Myers Squibb, Gilead, Janssen and Merck. MHN has received research support from and served as a consultant and/or advisory board member for Gilead Sciences, Janssen Pharmaceuticals and Bristol-Myers Squibb.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

Open Access This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

REFERENCES

1. Wiesner RH, Sorrell M, Villamil F. International Liver Transplantation Society Expert Panel. Report of the first International Liver Transplantation Society expert panel consensus conference on liver transplantation and hepatitis C. *Liver Transplan* 2003;9:S1–9.
2. Brown RS. Hepatitis C and liver transplantation. *Nature* 2005;436:973.
3. Gane EJ, Portmann BC, Naoumov NV, *et al.* Long-term outcome of hepatitis C infection after liver transplantation. *N Engl J Med* 1996;334:815.
4. Berenguer M. Systematic review of the treatment of established recurrent hepatitis C with pegylated interferon in combination with ribavirin. *J Hepatol* 2008;49:274.
5. Forns X, García-Retortillo M, Serrano T, *et al.* Antiviral therapy of patients with decompensated cirrhosis to prevent recurrence of hepatitis C after liver transplantation. *J Hepatol* 2003;39:389.
6. Burton JR Jr, O'Leary JG, Verna EC, *et al.* A US multicenter study of hepatitis C treatment of liver transplant recipients with protease-inhibitor triple therapy. *J Hepatol* 2014;61:508.
7. Nair SP. Protease inhibitor therapy post-liver transplantation in the treatment of hepatitis C virus infection. *Gastroenterol Hepatol (N Y)* 2013;9:388.
8. Faisal N, Yoshida EM, Bilodeau M, *et al.* Protease inhibitor-based triple therapy is highly effective for hepatitis C recurrence after liver transplant: a multicenter experience. *Ann Hepatol* 2014;13:525.
9. Coilly A, Roche B, Duclos-Vallée JC, *et al.* Management of HCV transplant patients with triple therapy. *Liver Int* 2014;34(Suppl 1):46.

10. Lawitz E, Sulkowski MS, Ghalib R, *et al.* Simeprevir plus sofosbuvir, with or without ribavirin, to treat chronic infection with hepatitis C virus genotype 1 in non-responders to pegylated interferon and ribavirin and treatment-naïve patients: the COSMOS randomised study. *Lancet* 2014;384:1756.
11. Suliman I, Pozza R, Kady Y, *et al.* The Combination of Simeprevir and Sofosbuvir for the Treatment of HCV Infection in Patients Post Liver Transplant With Significant Fibrosis [abstract]. *Hepatology* 2014;60(Suppl 1):545A.
12. Ripper SJ, Holt EW, Cooper S, *et al.* Simeprevir plus Sofosbuvir for Patients with Recurrence of Genotype 1 Hepatitis C Infection after Liver Transplantation [abstract]. *Hepatology* 2014;60(Suppl 1):684A.
13. Pungpapong S, Aql B, Leise M, *et al.* Multicenter experience using simeprevir and sofosbuvir with or without ribavirin to treat hepatitis C genotype 1 after liver transplant. *Hepatology* 2015;61:1880–6.
14. Nair SP, Dbouk N, Lingala S, *et al.* Safety and Efficacy of Simeprevir, Sofosbuvir, and Ribavirin Combination Therapy in Liver Transplant Recipients with Severe Recurrent HCV [abstract]. *Hepatology* 2014;60(Suppl 1):681A.
15. Lutchman GA, Nguyen NH, Hsiao TI, *et al.* Safety and effectiveness of sofosbuvir (SOF) in combination with simeprevir (SIM) or ribavirin (RBV) for the treatment of hepatitis C virus (HCV) recurrence after liver transplant (LT) [abstract]. *Hepatology* 2014;60 (Suppl 1):670A.
16. Gutierrez JA, Carrion AF, Avalos D, *et al.* Sofosbuvir and simeprevir for Treatment of Hepatitis C Virus Infection in Liver Transplant Recipients. *Liver Transpl* 2015;21:823–30.
17. Gordon FD, Kosinski AL, Coombs SJ, *et al.* Sofosbuvir + simeprevir is safe in liver transplant recipients [abstract]. *Hepatology* 2014;60 (Suppl 1):543A.
18. Ford RM, Pillai A, Cheng N, *et al.* Post-liver transplant treatment of hepatitis c with a combination of sofosbuvir, simeprevir, +/-ribavirin at a high volume academic transplant center [abstract]. *Hepatology* 2014;60(Suppl 1):701A.
19. Crittenden N, Davis EG, Marsano LS, *et al.* Single center experience with simeprevir/sofosbuvir combination therapy for recurrent hepatitis C virus infection in liver transplant recipients [abstract]. *Hepatology* 2014;60(Suppl 1):700A.
20. Reddy KR, Everson GT. Treatment of chronic hepatitis C with protease inhibitor-based therapy after liver transplantation. *Hepatology* 2013;58:1181.
21. Saab S, Greenberg A, Li E, *et al.* Sofosbuvir and simeprevir is effective for recurrent hepatitis C in liver transplant recipients. *Liver Int* 2015;35:2442–7.
22. Price JC, Terrault NA. Treatment of hepatitis C in liver transplant patients: interferon OUT, direct antiviral combos IN. *Liver Transpl* 2015;21:423–34.
23. Charlton M, Gane E, Manns MP, *et al.* Sofosbuvir and ribavirin for treatment of compensated recurrent hepatitis C virus infection after liver transplantation. *Gastroenterology* 2015;148:108.
24. Charlton M, Everson GT, Flamm SL, Jr, *et al.* SOLAR-1 Investigators. Ledipasvir and sofosbuvir plus ribavirin for treatment of HCV infection in patients with advanced liver disease. *Gastroenterology* 2015;149:649–59.
25. Najafzadeh M, Andersson K, Shrank WH, *et al.* Cost-effectiveness of novel regimens for the treatment of hepatitis C virus. *Ann Intern Med* 2015;162:407–19.
26. BVBA JID. *Efficacy and safety study of simeprevir in combination with sofosbuvir in participants with chronic hepatitis C virus infection without cirrhosis*. Bethesda MD: National Library of Medicine (US): ClinicalTrials.gov [Internet], 2014.
27. BVBA JID. *Efficacy and safety study of simeprevir in combination with sofosbuvir in participants with genotype 1 chronic hepatitis C virus infection and cirrhosis*. Bethesda MD: National Library of Medicine (US): ClinicalTrials.gov [Internet], 2014.
28. SC Liver Research Consortium LJ, LP. *SMV + SOF with/without RBV for IFN-II patients with CHC*. Bethesda MD: National Library of Medicine (US): ClinicalTrials.gov [Internet], 2014.
29. Janssen Scientific Affairs L. *An efficacy and safety study of simeprevir and sofosbuvir with and without ribavirin in participants with recurrent genotype 1 hepatitis C Post-Orthotopic liver transplant (GALAXY)*. Bethesda MD: National Library of Medicine (US): ClinicalTrials.gov [Internet], 2014.
30. AASLD/IDSA HCV Guidance Panel. Hepatitis C guidance: AASLD-IDSA recommendations for testing, managing and treating adults infected with hepatitis C virus. *Hepatology* 2015;62:932–54.