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Dear Editor,

we would like to thank you, the Editorial Board and the reviewers for the excellent and encouraging comments and constructive feedback about our manuscript. We hope, that we addressed all topics completely and satisfactory resulting in an improved manuscript that is appropriate and interesting for the readers of World Journal of Gastroenterology.

Please find below the point-by-point response to the remarks of the reviewer.

Thank you for your time and attention.

Yours sincerely,

Christian Rupp

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Reviewer 00722050:

COMMENTS TO AUTHORS

This prestigious work of Prof. Stremmel working group is pillar and has remarkable importance for the HCV infection platform and the direct-acting antiviral therapy.

Answer to reviewer 00722050

Thanks for this encouraging feedback about our manuscript.

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Reviewer 03538158:

COMMENTS TO AUTHORS

1. In abstract section: "Between January 2014 and December 2016, 39 patients with HCV reinfection after liver transplantation were treated at our tertiary referral center with sofosbuvir (SOF)-based regimens, including various combinations with interferon (IFN), daclatasvir (DAC), simeprivir (SIM) and/or ledipasvir (LDV). Thirteen patients were treated with SOF + IFN ± RBV. Ten patients were treated with SOF + DAC ± RBV. Eighteen patients were treated with fixed-dose combination of SOF + LDV ± RBV. One patient was treated with SOF + SIM + RBV. Three patients with relapse were retreated with SOF + LDV + RBV." These comments did not match with the text. 2. In Core tip section, what is "recirrhosis"??

Answer to reviewer 03538158:

Thanks for carefully reading our manuscript.

1. Regarding the numbers of patients in the abstract three patients with relapse were included in the eighteen patients treated with SOF + LDV ± RBV. As this information is a misleading formulation, we revised the abstract. Initially, fifteen patients were treated with SOF + LDV ± RBV. Additionally, all three patients with relapse after therapy with SOF + IFN ± RBV received SOF + LDV ± RBV. We corrected this information throughout our revised manuscript.
2. Recirrhosis should read recurrent cirrhosis. We corrected this wording throughout the revised version of our manuscript.

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Reviewer 01221188:

Major revision The patients treated with IFN and without IFN are mixed in this study. Therefore, the meaning of "all patients" is not clear. For instance, in page 9, SVR section, "all patients had attained SVR at 24 wk (SVR24)". However, three patients developed the recurrence with 4 wk after the end of treatment. Does "all patients" mean the patients treated without IFN? It might be better that the patients with treated IFN are excluded from the study. Minor revisions 1) When were the three patients experiencing relapse treated with fixed-dose combination of SOF + LDV? 2) The cause of re-transplantation is not clear. One was due to liver failure. What is the other's cause? 3) The liver histology and the source of infection should be added to table 1. 4) The dose of DAAs and PEG-IFN should be described in the text.

Answer to reviewer 01221188:

Thanks for this constructive feedback about our manuscript.

Major:

Of the thirty-nine patients, three patients experienced relapse after the first therapy with SOF + RBV, including those with (n = 1) or without (n = 2) the Peg-IFN for 24 wk. Relapse occurred within 4 wk after the end of therapy. All patients with relapse were retreated with fixed-dose combination of SOF + LDV and achieved SVR24. At the end of the study period, all thirty-nine patients had attained SVR at 24 wk (SVR24). We corrected the mistakable wording in the revised version of our manuscript.

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Minor:

1. None patient with fixed-dose combination of SOF + LDV experienced relapse, but only three patients treated with SOF + RBV, including those with (n = 1) or without (n = 2) the Peg-IFN for 24 weeks. All of the relapsed patients were re-treated with fixed-dose combination of SOF + LDV and achieved SVR24. We corrected this mistakable wording in the revised version of our manuscript.
2. Three patients have already been re-transplanted due to progredient liver failure due to HCV re-infection before initiation of DAA therapy. After successfully DAA therapy only one patient had to undergo liver transplantation and one patient died due to progredient liver failure. In both patients HCV was eradicated successfully. Obviously, in both patients treatment was to late to achieve recovery of liver function.
3. Liver histology was added to table 1. Source of infection were undetermined in our cohort.
4. The dosages were as follows: 400 mg sofosbuvir (SOF); pegylated (Peg)-IFN (180 μg once weekly, dosage modifications according manufacturers' recommendations) 60 mg daclatasvir (DAC), 150 mg simeprivir (SIM) and fixed-dose combination of 400 mg SOF with 90 mg ledipasvir (LDV). We included this information into the revised version of our manuscript.

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Reviewer 02441161:

COMMENTS TO AUTHORS

This excellent study written by Rupp C et al. has perfectly gone through the knowledge of the safety and efficiency of novel DAAs in liver-transplanted patients with recurrence of HCV infection in a real-world cohort at their tertiary care center. They found DAAs are safe and very efficient in HCV patients after liver transplantation, even in case of recirrhosis or history of relapse after pegylated-interferon therapy. The authors elucidate the therapeutic options that the high SVR rates, despite the many patients with recirrhosis, may argue for a 24-wk therapy period in patients with risk factors for therapy failure in a posttransplant setting. I thoroughly enjoyed reading this manuscript, especially, the outcomes that can be achieved. The manuscript comprehensively reviewed key articles addressed on this issue and well organized them. It should be of large interest for the readers of WJG, and I strongly recommend it to be published in the present form.

Answer to reviewer 02441161:

Thank you for this affirmative feedback about our project!

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Reviewer 00013080

COMMENTS TO AUTHORS

The article by Rupp et al is a retrospective analysis of the efficacy and safety of DDAs in pts who had undergone liver transplatation and had recurrent HCV infection. The articleiw well written Minor comments 1. why did the authors included only those with at had LT > 6-mo ? 2. how many pts had evidence of HCC before LT. More details regarding size of HCC 3. Why did the authors use SVR 24? do they believe that we need 24 w FU instead of 12w after the end of DDAs treatment?

Answer to reviewer 00013080:

1. As an internal standard at our department we did not start antiviral therapy in any liver transplanted patients before 6 months after LT. One reason was, that we wanted steroids to be tapered out completely, and immunosuppressive therapy reduced to the long-term dosage, as we were concerned about drug interactions at the beginning of DAA therapy. Furthermore, as we had no experience with side effects of DAA therapy and combined DAAs with interferon at the beginning of the study period we await clinical and laboratory recovery from LT. We included this important information in the revised version of our manuscript.
2. The majority of our patients had a history of HCC before LT (26/39 (66.7%)). All patients met the Milan-criteria (one lesion smaller than 5 cm; alternatively, up to 3 lesions, each smaller than 3 cm; no extrahepatic manifestations; no evidence of gross vascular invasion).

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3. In clinical practice we also use SVR12 to determine response to therapy. In this study we showed SVR24 rates, to rule out the possibility of delayed relapse in our patients, like rarely seen in patients treated with interferon and ribavirin. As all three relapses to DAA therapy appeared already within 4 weeks after cessation of therapy we believe SVR12 is sufficient to determine successful HCV eradication. We added this information to the revised version of our manuscript.