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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Hepatology
ESPS manuscript NO: 9585
Title: Efficacy and tolerance of Telaprevir and Boceprevir triple therapies in nonresponder HCV genenotype 1 patients with a severe liver fibrosis
Reviewer code: 00181443
Science editor: Xiu-Xia Song
Date sent for review: 2014-02-19 20:25
Date reviewed: 2014-04-04 17:30

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Rejection
[ ] Grade E: Poor		[ ] Existing	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

This manuscript by Bonnet et al. described the efficacy and safety of Telaprevir or Boceprevir therapy for treatment experienced patients with advanced fibrosis. The majority of patients were cirrhosis (F4 72%) and null-responder to prior therapy (63%), thus reflecting most difficult-to-treat patients. The results are encouraging showing high SVR rate in prior relapsers (80%) and even in null-responders (47%) with low rate of premature discontinuation due to SAE (8%) and no death. This information in real-life setting may be of value for physicians treating hepatitis C. 1. Patients were divided into relapsers and null-responders. It seems curious that no patient fell into category of partial responders, having 2 log HCV RNA reduction but HCV RNA detectable at EOT. Did the authors intentionally exclude these patients? 2. It may be informative if the authors could show the relationship between the high LS value and the incidence of SAE.

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Name of journal: World Journal of Hepatology
ESPS manuscript NO: 9585
Title: Efficacy and tolerance of Telaprevir and Boceprevir triple therapies in nonresponder HCV genenotype 1 patients with a severe liver fibrosis
Reviewer code: 02861401
Science editor: Xiu-Xia Song
Date sent for review: 2014-02-19 20:25
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Rejection
[ ] Grade E: Poor		[ ] Existing	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

This article attempts to assess the SVR rates to Telaprevir (TPV) or Boceprevir (BOC) in combination with PR in HCV genotype 1 patients with severe liver fibrosis Metavir F3 or F4 for whom had previously failed PR treatment in routine practice. The article is well-written, although most findings are well known. The authors claimed the overall 59.8% SVR rate was satisfactory, however this is very debatable. With the approval of sofusbuvir and the very nearly available interferon free combination therapies of DAAs, any 48-week therapy with SVR rate less than 60% seems not satisfactory. Moreover, the SVR rate observed in this study seems higher than well-controlled registration trials, especially for the 54.9% SVR rate in previous PR null responders treated with TVR. The SVR rates in previous PR null responders treated with PI/PR consistently observed in multiple registration trials were 30-38%. The 54.9% SVR in null responders and 44% SVR in null responders with cirrhosis were very unusual and may need more discussion. Other minor points: 1. Title: In general, relapsers are considered PR responders. And nonresponders generally include partial and null responders. 2. Because this is not a random trial, presentation of comparison between TVR and BOC based univariate analysis in the abstract is very misleading, especially when well-known significant baseline covariates were clearly imbalance between groups. 3. RVR is an early response variable. It generally affect by all important baseline factors. The correlation in your multivariate modeling should be state clearly. 4. How the optimal LS cut-off value of 21.3 kPa was derived should

be clearly specified. If this value is derived through a statistical cut analysis, the analysis should be described in the method section. 5. In your discussion section, you stated "Our 54 patients included null-responder to PR had an SVR of 44%, higher than that found in studies like REALIZE[8]." It is not clear where the 54 patients and 44% SVR refer to.