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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 18093
Title: NEW TREATMENT STRATEGIES FOR HEPATITIS C
Reviewer's code: 02943422
Reviewer's country: United States
Science editor: Ya-Juan Ma
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[Y] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This article is a review of the current therapeutic regimens using DAAs to treat chronic HCV infection caused by several genotypes of the virus. Overall, the article will be useful to gastroenterologists who treat HCV patients. The strength of this review article is that the optimal treatment regions for each of the HCV genotypes, 1a, 1b, 2, 3, 4, 5, and 6 are presented in a convenient summary. However the review article has a few weaknesses that should be addressed to increase the usefulness of this article for the audience of this journal. 1) The title of the paper refers to new treatment strategies for HCV. However, the strategies are not new since all of the DAAs discussed have been approved. If there is no intent to discuss other DAAs that are in preclinical and clinical development, the title of the paper should be changed to something like: "Current approaches to the treatment of multiple genotypes of HCV". However, it is the suggestion of this reviewer to keep the title as is and include more information on new treatment strategies in development thus providing the reader information regarding the HCV pipeline. Table 1 provides only a cursory listing of DAAs but gives no indication of what development stage they are in. Also, allisporivir is not a DAA and yet is included in Table 1 which is entitled Direct-Acting Antivirals. 2) To follow

this point, this review is limited to DAAs which inhibit HCV polymerase, protease, and NS5A. No mention is made of DAAs that target other HCV proteins such as the p7 or NS4B. For example, there have been numerous publications on inhibitors of NS4B and at least one clinical trial. To date there is no clinical proof-of-concept for NS4B inhibitors. Why not? It would be of interest to summarize this field for the reader and to provide the view of the authors regarding potential clinical utility of NS4B inhibitors. Furthermore, attempts to target the HCV IRES with ASOs and ribozymes have been made with little success. This area would also be of interest to readers of this journal 3) The discussion is very weak. The authors do not attempt to discuss future directions the field of HCV antiviral chemotherapy might take. Also, the authors facilely call for the reduction in the cost of DAA treatment but do not offer any ideas as to how a reduction in cost might be realized. Minor points: 1) 4th line of abstract: Ribavirin is more precisely a nucleoside analog. Also, it is not correct to say that ribavirin is a nucleoside inhibitor since its antiviral effect against HCV is not direct but rather is a result of its immunomodulatory activity. 2) Page 3, 17th line of the first paragraph. It is not clear what "affectivity" means unless the authors intended to use the word "efficacy". 3) Page 3, 1st line of the second paragraph: delete "thoroughly" since the term "eradicate" does not need to be modified by this adverb. 4) Page 4, lines 7-8 of second paragraph: St. John's Wort is a plant. It is more correct to write "hypericin, a component of the plant St. John's Wort". 5) Page 4, 3rd and 4th lines of second paragraph: change to, "….greater SVR than in patients with HCV genotype 1b;……" 6) Page 5, 10th line of second paragraph. The sentence should not begin with "81.3%". Rewrite to, "An SVR of 81.3% was achieved……." There are many instances in the manuscript where a sentence begins with a number as in this case. These should be rewritten. 7) Page 5, 1st line of last paragraph: change to, "……..NS5A inhibitor suppressing HCV RNA synthesis is a once-daily administered agent……" 8) Page 6, 1st line: change to, "As these are phase II studies, Daclatasvir is not expected….." 9) Page 7, 4th line, second paragraph: change "%47" to "47%". 10) Page 7, 22nd line of second paragraph: change "Other" to "Another". 11) Page 8, lines 4-5: change to: "Although mutations associated with resistance to Daclatasvir occur at several positions…." Also, it would be helpful to sta