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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 6485
Title: Safety and Efficacy of Hansenula-Derived Pegylated-Interferon Alpha-2a and Ribavirin Combination in Chronic Hepatitis C Genotype 4 Egyptian Children
Reviewer code: 02520511
Science editor: Wen, Ling-Ling
Date sent for review: 2013-10-22 15:55
Date reviewed: 2013-11-09 00:33

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

COMMENTS TO AUTHORS
Well done study. Presented in a detailed fashion. Though it is already known that extending treatment beyond 48 weeks achieves little extra benefit, your paper convincingly proves the case for Genotype 4 children (including prior non-responders) which is a not so widely studied sub-group. Specific comments: 1. Under "Study Population" - 5th line: Replace "Pepatology" with "Hepatology" 2. Under "Laboratory Investigations" - Consider avoiding the term "LFT". Please consider using the term "liver enzymes" or whatever is the lab that you are trying to indicate (?INR, albumin) 3. Please pay attention to column sizes in the tables. Some words had missing alphabets in Table 2 presumably due to discrepancy in column widths. 4. In discussion section, would add 2-3 lines about role of direct acting antivirals in this population in future because it appears that a majority of patients in this cohort are now non-responders to interferon based therapy.

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Title: Safety and Efficacy of Hansenula-Derived Pegylated-Interferon Alpha-2a and Ribavirin Combination in Chronic Hepatitis C Genotype 4 Egyptian Children
Reviewer code: 00031627
Science editor: Wen, Ling-Ling
Date sent for review: 2013-10-22 15:55
Date reviewed: 2013-11-15 14:23

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
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[ ] Grade E (Poor)		[ ] Existed	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
The aim of the study was to investigate the safety and efficacy of Hansenula-derived pegylated (PEG) interferon (IFN)-alpha-2a (Reiferon Retard) plus ribavirin customized regimen in 46 chronic hepatitis C genotype 4 infected Egyptian children. Only 11 out of 46 (23.9%) patients showed sustained virological response (SVR). Breakthrough was seen in 18 (39.1%) patients, one patient (2.17%) showed relapse and 14 (30.4%) were non-responders. Male gender, short duration of infection, low viral load, mild activity, and mild fibrosis were the factors related to better response. 5-day schedule did not affect response rate (1/17 had SVR). Treatment duration (whether 48 weeks or extended course to 72 weeks) gave similar response rates. Only mild reversible adverse effects were observed and children tolerated the treatment well. The Authors conclude that Reiferon Retard plus ribavirin combined therapy was safe. The study is interesting, however some major points could be addressed. 1- The Authors suggest: "The lower SVR in genotype 4 infected children in this trial compared to other trials in adults using the same IFN type and in children using other IFN types might be partially explained by the high percentage of previous non-responders included in the study (12/46). Of those 12 previous non-responders, only 2 showed SVR." To avoid this bias the results should be shown separately in patients with previous treatment with respect to those without. The type of previous treatments should be shown, and the interval time between previous and actual treatment could be shown and evaluated as a parameter that might influence SVR. 2- In Results Authors affirm: "They were all type 4, 65.2% were 4a and 17.4% were 4b. The genotype could not be determined in 8 patients". Please correct this apparent contradiction. 3- Please correct Tab. 2

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ESPS Manuscript NO: 6485
Title: Safety and Efficacy of Hansenula-Derived Pegylated-Interferon Alpha-2a and Ribavirin Combination in Chronic Hepatitis C Genotype 4 Egyptian Children
Reviewer code: 00504455
Science editor: Wen, Ling-Ling
Date sent for review: 2013-10-22 15:55
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[Y] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[Y] Grade E (Poor)		[ ] Existed	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
This paper is about the safety and efficacy of treatment for 48 or 72 weeks with a novel pegylated-interferon alpha 2a formula & ribavirin in Egyptian children with hepatitis genotype 4 or unknown genotype, who were treatment na?ve or previous non-SVR to interferon based therapy. My major issue with your study is that the hepatitis C genotype was not determined in 8 of 46 patients. A lot of the statements in the paper should be considered invalid as long as the hepatitis C genotype has not been determined for these 8 patients. It is very likely that the hepatitis C genotype will be 4, but I would like to see some proof. The paper needs to be restructured, and several key references are missing. Comments and suggestions 1. The title does not reflect the study. There were 2 different treatment groups, this should be mentioned. Hepatitis C genotype was not determined in all patients. Hence the current title s misleading. Some patients were non-SVR to previous IFN based treatment, this should be mentioned. 2. Has this study been registered in one of the clinical trial databases such as www.clinicaltrials.gov ? Please provide the link to the record. Please register the study if it hasn't been registered. 3. The abstract is too long, 556 words. Please reduce to about 300 words, or whatever the limit is for this journal. 4. Please restructure the abstract and describe methods and results in a logical sequential order. 5. Please describe the aim, the patient group (na?ve and previous non-SVR), the 2 treatment groups clearly. 6. Please provide a word count for the manuscript. I now count 3476 words (good). 7. Manuscript thoughout: There is a tendency to refer to too many papers. It would make more sense to refer multiple times to a few standard references. Sometimes it is not obvious why a certain reference was chosen, such as references 1, 9, 11, 17. 8. Introduction paragraph 2: Blood transfusion is NOT "the principal route

of transmission in children". The paper you quote describes a highly selected group of children in a resource poor setting. Please refer to a more general review article on hepatitis C infection in children. Table 3 also contradicts your statement. It's certainly important, but it's not the principal route. 9. Introduction paragraph 2: Perinatal transmission is important for this paper, can you elaborate? See PMID: 19382251 10. Introduction paragraph 3: The first sentence should be the last sentence of paragraph 2. 11. Introduction paragraph 3: The rest of the paragraph is difficult to read. 12. Introduction paragraph 3: The last sentence, why choose reference 11 and not a standard paper or a paper that described all definitions, EVR, RVR, SVR, non-SVR, breakthrough, relapse, etc? 13. Introduction paragraph 5: Can you be more specific and lead us to pediatric hepatitis C? 14. Introduction paragraph 6: Can you reference the registration trials? 15. Introduction paragraph 7: Redundant. Please remove. 16. Materials and Methods: Please remove all numbers of patients from materials and methods. How many patients were enrolled, treated in which arm, and came from which centers should be regarded as results and describe in the results section. Here please describe your materials and methods but no numbers. 17. Materials and Methods paragraph 5 & 6: Group I and group II. I don't understand how you grouped your patients and treated them. How can you group patients who are HCV-RNA negative at week 12 and patients with a < 1 log decrease in HCV-RNA in 1 group? Please describe this in a logical sequential order. 18. Materials and Methods paragraph 7: The last sentence is redundant. You also describe the laboratory investigations in paragraph 8. 19. Materials and Methods paragraph 9: Please divide into two paragraphs. If you use the definitions from reference 21 you can omit reference 11 and substitute that with 21, see my earlier comment. 20. Materials and Methods paragraph 9 and throughout paper: