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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 7417
Title: Heparanase Inhibitor PI-88 as an Adjuvant Therapy for Hepatocellular Carcinoma After Curative Resection: A 3-Year Follow-Up Study
Reviewer code: 00504345
Science editor: Gou, Su-Xin
Date sent for review: 2013-11-18 14:46
Date reviewed: 2013-12-11 17:31

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[Y] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[Y] Accept
[ ] Grade B (Very good)	[Y] 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

1. Please, check again the spelling of some words (to many merged inscribed words!). 2. It is important to make clear whether the patients were receiving other therapy during the follow period. 3. Please, it would be correct to mention again the PI-88 drug form and the pharmaceutical manufacturer.

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Title: Heparanase Inhibitor PI-88 as an Adjuvant Therapy for Hepatocellular Carcinoma After Curative Resection: A 3-Year Follow-Up Study
Reviewer code: 00502903
Science editor: Gou, Su-Xin
Date sent for review: 2013-11-18 14:46
Date reviewed: 2013-12-19 01:19

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[Y] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
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COMMENTS TO AUTHORS

The authors present an important follow-up study of outcomes following PI-88 treatment as adjuvant therapy for hepatocellular carcinoma. The study is well done and well-presented. After 9 treatment cycles over 36 weeks, no additional PI-88 treatment was administered until 156 weeks. Regarding the study design, it is not clear how other treatments or medications were handled during the extended follow-up period. If that data is available, it would be helpful for evaluation of the treatment effects. How was compliance with the study regimen evaluated? The authors note that PI-88 at 250 mg/day was associated with adverse effects that resulted in dropout, but were subjects who remained on that dose also less compliant? Findings of the study included persistent benefits in time to recurrence and disease free survival over the 3 year study. Overall survival was not affected. Subgroup analyses demonstrated improved disease free survival in the higher risk cohort. Overall, the limitations for analysis of a reduced sample size in this follow-up study are understood. However, in spite of this decreased power, more comprehensive reporting of statistics needs to be presented in the Results, especially p-values and confidence intervals. For the most part, the Discussion is well-written. However, the length and exuberance may be tempered. For instance, the brief paragraph on PI-88's role as a cytostatic agent seems redundant when the next paragraph contains an excellent summary of potential mechanisms and interactions that would bolster PI-88's effect. The Tables provide important data but need to be more clearly labeled and include relevant p-values. I presume that the values in Table 1 are presented as mean (%) for every row except Age (year), but that needs to be made clear. Also, I presume that ITT stands for intention-to-treat, but

please specify. Table 2 notes more frequent adverse events in the 250 mg/day group. P-values or confidence intervals are needed for the differences observed in Tables 2 and 4. The References and Figures are ok.

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Reviewer code: 00007472
Science editor: Gou, Su-Xin
Date sent for review: 2013-11-18 14:46
Date reviewed: 2014-01-03 03:04

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

COMMENTS TO AUTHORS

Authors here provide additional information from continued follow-up of the majority of patients recruited into an already published phase II trial that suggested a potential benefit of the heparanase inhibitor PI-88 as an adjuvant therapy for HCC. The results further suggest this potential effect although the strength of the evidence is somehow smaller due to intrinsic design problems. They include treatment compliance as well as access to other therapies. The impact is not minor since authors did not observe a difference in overall survival, and I feel that discussion of these limitations should be reinforced. Also, the potential impact of side effects in compliance deserve discussion since they are higher among patients receiving higher doses. 95%CI should be reported in the results section.