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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 11393

Title: Prophylaxis Against HBV Recurrence After Liver Transplantation: A Nationwide Multicenter Study

Reviewer code: 00013338

Science editor: Su-Xin Gou

Date sent for review: 2014-05-20 18:04

Date reviewed: 2014-07-03 18:25

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

the paper by Jiang et al. reports on the results of the China Liver Transplant Registry on HBV prophylaxis in patients receiving liver transplantation. They conclude, that a lower dose of HBIG plus Adefovir or Entecavir or Lamivudine results in excellent treatment response, especially the combination HBIG/Entecavir. The paper is well written and of highly clinical implications. Therefore, I recommend publication without any changes.



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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 11393

Title: Prophylaxis Against HBV Recurrence After Liver Transplantation: A Nationwide Multicenter Study

Reviewer code: 00054120

Science editor: Su-Xin Gou

Date sent for review: 2014-05-20 18:04

Date reviewed: 2014-05-30 00:50

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

same as above

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 11393

Title: Prophylaxis Against HBV Recurrence After Liver Transplantation: A Nationwide Multicenter Study

Reviewer code: 00743117

Science editor: Su-Xin Gou

Date sent for review: 2014-05-20 18:04

Date reviewed: 2014-06-20 22:13

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The manuscript entitled, "Prophylaxis against HBV recurrence after liver transplantation: A nationwide multicenter study" by Shen S et al., performed a database study of Chinese liver transplant registry regarding the prophylaxis for hepatitis B recurrence with the combination treatment of the intramuscular hepatitis B immunoglobulin (HBIG) administration and antiviral nucleot(s)ide analogues. They reported the patient survival and hepatitis B recurrence after liver transplantation according to the different nucleot(s)ide analogues (lamivudine, entecavir, and adefovir), and investigated the factors associated with hepatitis B recurrence. I have some comments. Comments 1. The intramuscular administration of HBIG should be clarified in the abstract, since intramuscular HBIG is not prevalent worldwide. 2. This is the database study of registry. This should be clarified in the title. 3. Adefovir and entecavir were used in recent cases according to the figures. I recommend authors to use the data after the introduction of these drugs, meaning that cases with lamivudine in earlier days had better be excluded from the study. This can minimize the learning curve bias. 4. How was HBs-Ab titer? Was there any lower limit? Anyway, authors should discuss about the HBs-Ab titer monitoring. 5. Please refer to Am J Transplant 2013; 13:353. There many other studies of the combination prophylaxis with HBIG and entecavir. 6. Please change the scale of the vertical axis of Figure 3 to make the difference very obvious. 7. The descriptions in "Patient survival" and "HBV recurrence" in Results are redundant. 8. I wonder how the authors



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checked the adherence to the combination prophylaxis in this cohort. Was it possible to confirm the adherence of each patient based only on the registry database?



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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 11393

Title: Prophylaxis Against HBV Recurrence After Liver Transplantation: A Nationwide Multicenter Study

Reviewer code: 01560498

Science editor: Su-Xin Gou

Date sent for review: 2014-05-20 18:04

Date reviewed: 2014-06-22 20:43

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input checked="" type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

Authors reported that low-dose intramuscular HBIG plus one nucleoside analogue provides an effective prophylaxis against posttransplant HBV recurrence, especially for HBIG plus entecavir. Sample number is enough, and this is national-wide study in China. This paper is well-written, and this report is informative for readers in this field.



ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 11393

Title: Prophylaxis Against HBV Recurrence After Liver Transplantation: A Nationwide Multicenter Study

Reviewer code: 00053868

Science editor: Su-Xin Gou

Date sent for review: 2014-05-20 18:04

Date reviewed: 2014-06-23 15:22

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The authors of the present manuscript have reviewed a large database in order to study the effectiveness of nucleos(t)ide analogues + low-dose intramuscular HBIG in the prophylaxis of recurrent hepatitis B after liver transplantation. They conclude that this a very effective strategy, specially when entecavir is used. This is a very interesting topic, because HBV is a frequent indication of liver transplantation and the most cost-effective prophylaxis is a matter of debate. The manuscript has some details that should be reviewed: ? In the introduction, the authors mention that the proportion of patients transplanted for hepatitis B is very high (78%). I think the worldwide proportion is lower. ? It is suprising to find that tenofovir prophylaxis has not been studied. ? As the results come from a large database, it is not clear is the nucleos(t)ide analogue + intramuscular HBIG have been maintained for the whole period of study. ? Most of the patients included in the database have been excluded, restricting them to those patients who are on treatment with a nucleos(t)ide analogue + intramuscular HBIG. With the exclusion of these patients, the manuscript could only be focused to the comparison between lamivudine, entecavir and adefovir when it is combined with low-dose intramuscular HBIG. They do not answer two important questions: 1) Is low-dose intramuscular HBIG as effective as intravenous HBIG (in combination with nucleos(t)ide analogues)?, and 2) Is any HBIG necessary if adefovir or entecavir are used? ? Patients have been recruited between January 2000 and December 2009. In the first part of the database, all the patients should



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have been treated with lamivudine (because adefovir and entecavir were not available). So, they should be excluded. ? The groups are different between them in some important points such viral load, duration of pre-transplant treatment. It could be of interest to compare the rates of recurrence with each strategy in patients with low viral load and in patients with high viral load. ? The information given in figure 2 and table 2 is repetitive. ? The information given in figure 3 and table 3 is repetitive. ? The comparison between group B and group C does not show significant differences in the recurrence rates between them (the differences between them are only found in the long-term, when a small number of recurrences increases the rate). The authors should temper they discussion for the use of entecavir (ETV plus HBIG may be considered as first-line therapy...). ? In the discussion, the authors suggest that intramuscular HBIG should be preferred to intravenous HBIG because of its high efficacy and lower price. The study has not been designed to compare them; thus, the discussion about this comparison should be avoided. ? The authors have found that patients transplanted for HCC have a higher HBV recurrence rate. They suggest that occult metastases could be a reservoir of HBV. Have they found if patients with recurrent hepatitis B have a higher risk of recurrent HCC?