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## ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Hepatology

**ESPS manuscript NO:** 12268

**Title:** Nucleos(t)ide Analogues to Treat Hepatitis B Virus-Related Hepatocellular Carcinoma After Radical Resection

**Reviewer code:** 02438878

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2014-07-01 08:33

**Date reviewed:** 2014-07-08 12:07

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" 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

This review systematically summarized the literature since 2004 on outcomes after administering NAs to patients with HBV-related HCC following radical resection. This is a good review that provide evidence for clinicians that patients with HCC should strongly consider NA therapy if they are positive for HBV-DNA, and that the available evidence suggests that postoperative NA therapy can increase both recurrence-free and overall survival. The results may have implications in the treatment of HBV-related HCC.



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		<input type="checkbox"/> No records	

**COMMENTS TO AUTHORS**

Je et a in their paper entitled “Nucleos(t)ide analogues to treat hepatitis B virus-related hepatocellular carcinoma after radical resection” present a very important message that have been attracting attentions among those who are involved in the management of HBV-HCC. With an increasing number of reports coming from Asian countries on this subject, it appears that antiviral therapy for HBV-HCC following surgical resection may offer a potential alternative to liver transplantation for the early HCC. While liver transplantation has been the choice of treatment for the early stage HCC, now there may be choices between antiviral therapy after local resection (or ablation) versus liver transplantation. This availability is significant in view of the constant shortage of liver graft and the expenses involved in the liver transplantation.

With the authors’ thorough review and analysis of hitherto published data, it is likely that postoperative antiviral (NA) therapy for patients with HBV-HCC would be widely used.

Comments

1. While the authors quoted reports only from Asia, there was one similar report from the United States. It has a small number of patients appeared first in 2011 (Int J Cancer 128:739-42) and further follow up published in 2014 with more cases and a longer follow up of over 12 years (Cancer Med 3:390-6).
2. In this paper, the authors reported HCC patients who received surgical resection only (which is curative) in this paper. However, with the currently advanced techniques of the loco-regional ablations such as microwave ablation, Radiofrequency ablation (RFA), Transarterial chemoembolization (TACE), radioembolization and others, the same approach (NA therapy) applies for HCC patients who underwent such procedures in addition to surgical resection. These experiences are included in the paper from the US mentioned above. Therefore, conclusion may/should include those with ablative procedures while resection remains the major and most commonly used procedure in Asia.
3. As to the treatment criteria with NA for chronic hepatitis B, authors quoted only those from Asian-Pacific Consensus, AASLD, and Chinese J Hepatol. Since this paper and recommendation will be read worldwide, other known and widely used guidelines should also be included. For example, there are the treatment Algorithm in USA by Keeffe et al (Clin Gastroenterol, Hepatol 2006) and Asian American Guideline (Dig Dis Sci 2011; 56:3143-62) and the EASL guideline in Europe. It would be better to include all for the healthcare providers/readers in different parts of the world.

In these guidelines, the criteria for starting treatment such as the ALT level, HBV DNA amount, for HBeAg (+) and HBeAg (-) patients and stopping time for

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HBeAg patients after seroconversion vary depending on the guidelines. Also is the length of therapy for HBeAg (-) patients. Since these points are very important, authors are advised to carefully delineate these various criteria in the section of "Indications and duration of NA therapy after surgery". Certainly, in this section, there are areas where some physicians may not agree with the recommendations quoted by the authors regarding the NA treatment for HBV patients.

4. In the same section indications and duration of NA therapy, in the second Paragraph, authors mention that 'for HBeAg (-) patients, after 2 years of therapy even if HBsAg is positive, therapy can be discontinued if HBV DNA is negative on three separate occasions 6 months apart'. Please, provide reference for this statement.
5. The last paragraph in the same section is very important. Also the conclusion is well justified.



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