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Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6592

Title: Development of Systemic Therapy for Hepatocellular Carcinoma at 2013: Updates and Insights

Reviewer code: 00053731

Science editor: Ma, Ya-Juan

Date sent for review: 2013-10-25 19:20

Date reviewed: 2013-11-09 20:10

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 type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This is a well-written review on the systemic treatment options for advanced stage HCC from well-known and respected authors. There are several issues that need some attention (see below) but I think they could be solved easily. Specific comments: -BRISK-FL: it should be mentioned that this was a non-inferiority design and that the goal of non-inferiority for brivanib was not reached (leading to the discontinuation of the brivanib-program) -page 10 HDAC: please check the description of the mechanism of action: seems to be a mistake (less condensed-inactivation of gene transcription?) -page 13, first sentence: does not make sense, please check (patient population?) -Combination treatments: it is not correct that the study by Melanie Thomas in the end yielded impressive result. The JCO publication was only an interim analysis, the final publication was much less impressive (Kaseb et al., Oncology 2012; 82: 67; please present this as well/instead). So it is not surprising to see another study (ref. 57) showing much less impressive results. -chemotherapy, page 14: it should be noted that the EACH study did not include a control arm (sorafenib or at least placebo), so it only proved that it was less toxic than the comparator regimen. So far, no chemotherapy regimen was ever able to show a survival advantage in any stage of HCC. Unfortunately, the anti-tumor activity seems to be offset by the hepatotoxicity. -page 16, TACE-combinations: it is incorrect that the SPACE trial did not yield a significantly positive effect in the TTRP, since the predefined p-value for the one-sided log-rank test was set at 0.15; so the trial is a positive trial from a statistical point of view. It is however true that nobody is impressed by the results. Please also rephrase page 16, since the results were not "negative" but certainly "discouraging" or "unimpressive". -page 17: the description of the BCLC stage C is inaccurate, please improve -staging systems: references 72 and 74 are the same manuscript and this is of



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extremely poor quality (reasons are given in commentary in J Hepatol 2012; 56: 488) and misleading: this manuscript should never be cited or used as an argument for a staging system. It is very important to distinguish between "prognostic systems" (not the primary intention of BCLC but also useful to some extent) and "treatment staging systems" like BCLC -page 18: a comment on selection tools for selection patients for TACE (e. g. ART-score, Hepatology 2013) might be reasonable here -references: please check for current citation; a manuscript published in 2011 (e. g. ref. 57) can be cited with the full reference, not only with the DOI.



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Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6592

Title: Development of Systemic Therapy for Hepatocellular Carcinoma at 2013: Updates and Insights

Reviewer code: 00052607

Science editor: Ma, Ya-Juan

Date sent for review: 2013-10-25 19:20

Date reviewed: 2013-12-01 23:02

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"/> Existed	<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	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

This is a well-written and detailed review about the current status of systemic therapy, including combination therapy and future direction, for HCC. This review paper is suitable for publication on WJG.



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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6592

Title: Development of Systemic Therapy for Hepatocellular Carcinoma at 2013: Updates and Insights

Reviewer code: 00012386

Science editor: Ma, Ya-Juan

Date sent for review: 2013-10-25 19:20

Date reviewed: 2013-12-04 07:34

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"/> Existed	<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"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This article seems well-written and looks important in this field. This article would give us an new information for the systemic chemotherapy for HCC.



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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6592

Title: Development of Systemic Therapy for Hepatocellular Carcinoma at 2013: Updates and Insights

Reviewer code: 00001558

Science editor: Ma, Ya-Juan

Date sent for review: 2013-10-25 19:20

Date reviewed: 2013-12-09 10:24

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"/> Existed	<input type="checkbox"/> High priority for publication
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<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This review article described recent results of systemic therapy for HCC, especially for the molecular targeting ones. The contents are interesting and informative for the clinicians. This manuscript is basically acceptable at the current form. However, references should be updated and should be changed to the correct form (for example, sometimes "J Clin Oncol", but sometimes "Journal of Clinical Oncology"). The reference number in the Table 1 might be wrong and should be corrected (Ref 83-85 are not included in the reference section).



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Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6592

Title: Development of Systemic Therapy for Hepatocellular Carcinoma at 2013: Updates and Insights

Reviewer code: 00012156

Science editor: Ma, Ya-Juan

Date sent for review: 2013-10-25 19:20

Date reviewed: 2013-12-11 17:33

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 type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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
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<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
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COMMENTS TO AUTHORS

Chen et al. described the review of systemic therapy for HCC up to 2013. The contents are elaborated and references are new, therefore, this paper is worthwhile for the doctors who treat the HCC patients.