

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 25285

Title: Clinical analysis of patients with hepatocellular carcinoma recurrence after living-donor liver transplantation

Reviewer's code: 00504591

Reviewer's country: Japan

Science editor: Jing Yu

Date sent for review: 2016-03-04 08:44

Date reviewed: 2016-03-07 09:21

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<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"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

This is a retrospective study of the recurrent hepatocellular carcinoma (HCC) after living donor liver transplantation (LDLT) among 54 patients with recurrent HCC out of 293 LDLT recipients with HCC. Overall findings were very similar to those obtained in previous reports. The finding that the combination treatments of sorafenib and an mTOR inhibitor could have survival benefits in patients with recurrent HCC who could not undergo the curative treatment is worthy of notice.

Comments

1. The institutional criteria for LDLT for HCC (beyond the Milan) should be clarified.

: Because of a shortage of deceased donor in my country, most patients with HCC could not undergo DDLT, and usually underwent LDLT. Therefore, For LDLT, relatively expanded selection criteria could be adopted, if liver transplantation was not contraindicated such as distant metastasis, regional lymph node metastasis, and macroscopic main portal vein invasion. In case of HCC patients beyond Milan criteria, when the tumor biology is expected to good and the donor is available, we performed LT first, but otherwise we performed locoregional treatments with the purpose of bridging or down-staging.

2. Patient characteristics of all cohort should be presented in a table stratified by within/beyond Milan.

: Table 3 showed that differences of patients characteristics and HCC recurrence patterns according to the Milan criteria at transplantation.

3. Figure 1. Vertical axis is not “cumulative recurrence rate”. For the comprehensiveness, the actual “cumulative recurrence rate” should be shown as figures. The ratio of patients developing recurrent disease within 1- and 2-year among patients with recurrent HCC may be enough to be described in the text.

: Because we studied only 54 patients with HCC recurrence after LDLT, we showed “proportion of HCC recurrence” in Figure 1. We modified “Cumulative recurrence rate” to “Proportion of HCC recurrence” in Figure 1.

4. The rate and the profile of adverse event among the combination treatment (sorafenib and sirolimus) group should be presented.

: During the combination treatments of sorafenib and sirolimus, adverse effects included 8 cases of diarrhea and 3 cases of hand-foot syndrome. Although the combination treatment was generally well tolerated, there were adverse events exceeding grade 3 were 3 cases of diarrhea.

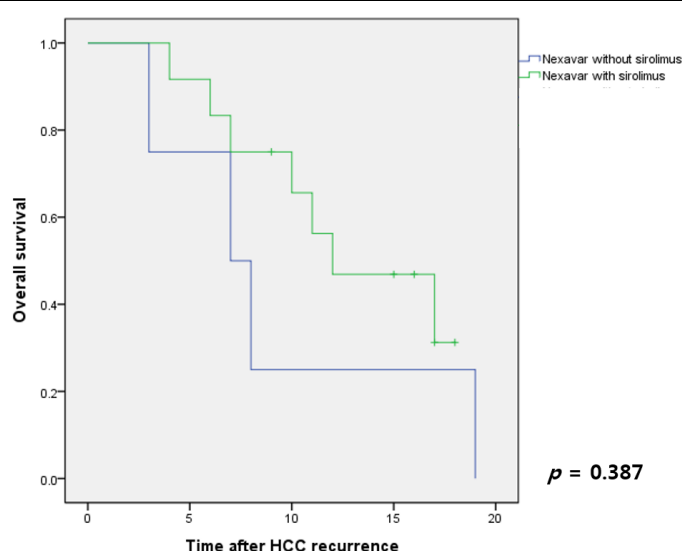
5. How was the adherence to the combination treatment?

: One patient discontinued the combination treatment, the remaining two patient reduced the dose of sorafenib.

6. Were there patients with sorafenib without sirolimus among palliative treatment group? Reading the text, from 2008 to 2012, those with palliative treatment for recurrent HCC might had been treated as such. In that case, these patients should be separately presented and compared.

: Since the introduction of sirolimus in 2012 in our hospital, 4 patients received sorafenib treatment without sirolimus.

In palliative group	n	Mean survival	Median survival	p - value
Nexavar without sirolimus	4	9.25 ± 3.425	7.0 (range: 3.0 – 19.0)	0.387
Nexavar with sirolimus	12	12.79 ± 1.486	12.0 (range: 4.0 – 18.0)	



7. Table 4. Please demonstrate the performance of other treatment such as TACE, radiation, and operation.

: Most HCC recurrent patients received not only single treatment but also combination treatments (operation, TACE, nexavar, and radiation). In our study, most recurrent patients received combination treatments especially in palliative group. And the study population was very small. Therefore, we could not compare the performance of other treatment such as TACE, radiation, and operation. We also know the weakness of this study. Because of small sample size and short follow up period, we could not perform the multivariate analysis for effectiveness of combination treatment of sorafenib and sirolimus. Lastly, prospective studies with larger cohorts are required to address these issues more fully.

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Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 25285

Title: Clinical analysis of patients with hepatocellular carcinoma recurrence after living-donor liver transplantation

Reviewer's code: 03537089

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Science editor: Jing Yu

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<input type="checkbox"/> High priority for publication
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<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

The required corrections after revision

1- The corrections are red colored in the manuscript

: We corrected the manuscript according to the reviewer's opinion.

2- Where is list of abbreviations?

: We added list of abbreviations.

3- In the abstract: see the red colored in manuscript

: We corrected the manuscript according to the reviewer's opinion.

4- In the introduction: see the red colored in manuscript

: We corrected the manuscript according to the reviewer's opinion.

5- In patients and methods: see the red colored in manuscript

: We corrected the manuscript according to the reviewer's opinion.

6- In patients and methods, the author did not mention the consent regarding operations and researches

: We added the informed consent statement in the title page of the manuscript.

7- Taper of steroid 3 months not 1 month after LT

: We corrected the steroid tapering schedule in the methods page of the manuscript.

8- There is defect in follow up data (mean or median, and range)

: The median follow up period was 18.5 months (range: 3–170 months), and we added this information in the methods page of the manuscript.

9- During the follow up, and because, this is a retrospective study, I think, there will be a missing data, how many patients excluded due to missing data, the author did not mention

: Although this study was a retrospective study, no one patients failed to follow up among 53 patients.

10- The last red colored paragraph in patients and methods should be a part of results not patients and methods.

: We corrected the manuscript according to the reviewer's opinion.

11- Again, in the last underlined red colored paragraph of patients and methods, the numbers in the palliative group should be corrected (The total is 39 not 31)

: We added the table about treatment modalities for recurrent HCC after LT (Table 2).

12- In Statistical analysis: see the red colored in manuscript

: We corrected the manuscript according to the reviewer's opinion.

13- What is this (?2)? In statistical analysis.

: Pearson's chi-square test. We corrected the manuscript.

14- In results, see red colored corrections in the manuscript.

: We corrected the manuscript according to the reviewer's opinion.

15- In discussion: see the red colored in manuscript

: We corrected the manuscript according to the reviewer's opinion.



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16- In conclusion: see the red colored in manuscript

: **We corrected the manuscript according to the reviewer's opinion.**

17- In references: see the red colored in manuscript

: **We corrected the manuscript according to the reviewer's opinion.**

18- In tables: see the red colored in manuscript

: **We corrected the manuscript according to the reviewer's opinion.**