Format for ANSWERING REVIEWERS

September 30, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5399-review.doc).

Title: Iodine-131–Labeled Metuximab Combined with Chemoembolization for Unresectable Hepatocellular Carcinoma versus the Chemoembolization

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Name of Journal: *World Journal of Gastroenterology*

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The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) Did the authors perform a prospective trail or is this a retrospective analysis?

It is a nonrandomized prospective Cohort study and the online Registration number is ChiCTR-TNRC-12002921. I have added in the manuscript.

(2) They do not provide specific data for the endpoints of their study?

We actually provided the specific data for the endpoints of our study in the third paragraph of page 7 and table 4

(3) What was the statistical basis for number of patients included for example?

We used “Freedman model” to calculate the number of patients needed for our trail and the result was 183 that was less than the patients enrolled in our trail (185).

(4) The authors need to provide more details on their patients to exclude any imbalances. Basically absolute numbers for liver functions test including bilirubin, INR and platelets, AFP values, percent of vascular invasion, metastasis, size of tumor (size larger than 10cm).

We had provided absolute numbers of percent of vascular invasion in the first paragraph of page 8 that was 35.79% (34/95) in test group and 33.3% (30/90) in control group.

As to the size of tumor(larger than 10cm): In clinical practice , we usually used the criterion of Barcelona Clinic Liver Cancer that was 5cm . When the tumor size was beyond 5cm, it was the number and metastasis affected the patients’ prognosis much more than the pure tumor size.

As to the absolute numbers for bilirubin, Platelets, AFP values, et al. It is too much tables if we provide all the absolute numbers that may confuse the reader .so, we provided the final result directly. The following were the absolute numbers.

1. TB

Obs	**Control group**	Test group
Before therapy	19.1	14.8
After therapy	19.55	15.5
The D-value between therapy	0.95	1.7

Test Statistics(a)

	Before therapy	**After therapy**	**The D-value between therapy**
Mann-Whitney U	3511.500	2074.000	2302.000
Wilcoxon W	7789.500	4775.000	4858.000
Z	-1.653	-1.413	-.177
Asymp. Sig. (2-tailed)	.098	.158	.860

a Grouping Variable: group

2. Platelets

Obs	**label**	**Control group**	Test group	**test**	**pvalue**
Before therapy	PLT1	141.29±88.05	143.27±76.69	t= -0.1617	0.8717
After therapy	PLT2	142.02±82.37	103.53±62.75	t= 3.0582	0.0028
The D-value between therapy	d_PLT	12.74±52.59	-36.69±49.62	t= 5.6598	<0.0001

3. AFP

Obs	Control group	Test group
Before therapy	304.8	350
After therapy	336.6	236.6
The D-value between therapy	0	0

Test Statistics(a)

	Before therapy	**After therapy**	**The D-value between therapy**
Mann-Whitney U	3964.500	2150.000	2102.500
Wilcoxon W	7705.500	4166.000	4587.500
Z	**-.353**	**-.253**	**-.152**
Asymp. Sig. (2-tailed)	**.724**	**.800**	**.879**

a Grouping Variable: group

The D-value between therapy

group * AFP_degree Crosstabulation

			AFP_degree			Total
			decrease	stable	increase	
group	control	Count	19	19	23	61
		% within group	31.1%	31.1%	37.7%	100.0%
	test	Count	19	23	28	70
		% within group	27.1%	32.9%	40.0%	100.0%
Total		Count	38	42	51	131
		% within group	29.0%	32.1%	38.9%	100.0%

Test Statistics(a)

	AFP_degree
Mann-Whitney U	2048.000
Wilcoxon W	3939.000
Z	**-.427**
Asymp. Sig. (2-tailed)	**.669**

a Grouping Variable: group

(5) They should provide more precise data on time between TACE procedures, treatments during follow-up (RFA, ethanol injection and Sorafenib).

We had mentioned these in the second paragraph of page 5 and the second paragraph of page 6. Those were "The patients were suggested to local ethanol injection, microwave coagulation, resection or liver transplantation before and after TACE or Licatin therapy if needed." and "After treatment, ultrasound、CT scan or MRI was performed every 1 ~ 3 months with or without contrast enhancement to evaluate the features of Lipiodol deposit and the therapeutic effect according to the response evaluation criteria （RECIST） for solid tumors. If elevated tumor marker (AFP), diminished Lipiodol, enlarged lesions or new nodules were observed, the patients were readmitted for angiography and treatment."

(6) Reasons to stop TACE + 131I-metuximab and how many patients switched arms (and why) and why and how many patients were suspended treatment TACE + 131I-metuximab?

We had mentioned these in the third paragraph of page 7.

In fact, in clinical practice, the doctor only has the right to suggest when to start or stop therapy. It is the patients themselves who decided whether and when to stop TACE + ^{131}I-metuximab).

In our trail, about 14 patient in test group lost follow up and that number in control group

was 0. The reason might be that patients who received combined therapy were superior to those of control group in economy ability .they had more money to offer for other therapies in other places. When they decided to receive therapies elsewhere, they often refuse to been followed up in anyway. Of cause, some of them might die .so the telephone number left were waste and could not been followed up. These were very common in china.

(7) Did the more intense therapy affect the liver reserve?

We wouldn't offer the patients intense therapy as we mentioned in the second paragraph of page 6 : "After treatment, ultrasound、CT scan or MRI was performed every 1 ~ 3 months with or without contrast enhancement to evaluate the features of Lipiodol deposit and the therapeutic effect according to the response evaluation criteria （RECIST） for solid tumors. If elevated tumor marker (AFP), diminished Lipiodol, enlarged lesions or new nodules were observed, the patients were readmitted for angiography and treatment."

(8) How do the authors explain that almost 50% of the patients in the TACE group died within 6 months? mOS in this group is very short and is nowadays seen in second line clinical trials of patients after Sorafenib failure.

Because they are very late HCC patients as I mentioned in the second paragraph of page 7, those patient always have few choice of treatment and often very poor prognosis. Patients like these were seldom enrolled into clinical trials before.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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