

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 55265

Title: Efficacy and Safety of Lenvatinib for Patients with Advanced Hepatocellular Carcinoma: A Novel Real-World Study Conducted in China

Reviewer's code: 05246416

Position: Peer Reviewer

Academic degree: MD

Professional title: Assistant Professor, Attending Doctor

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2020-03-14

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-03-15 18:40

Reviewer performed review: 2020-03-15 21:06

Review time: 2 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is a report of a retrospective study on a systemic therapy, lenvatinib, in hepatocellular carcinoma patients in China. Results from this real-world study are comparable to existing data. The use of this systemic therapy medication appeared safe and effective. The analysis of genetic mutation in the treatment response is quite intriguing. Perhaps a prospective study could further investigate this topic. The "strict" eligibility criteria were quite vague; authors did Not specify inclusion criteria specifically, though exclusion criteria were somewhat hinted--31 patients excluded due to prior treatment w/ another "anti-tumor therapy" and 26 were excluded due to additional concurrent "anti-tumor therapy," which I assume is another systemic therapy. They need to clarify by stating that the so called "anti-tumor therapy" is systemic therapy, since they appeared to include patients with locoregional therapy. One major issue with the omission of the inclusion criteria is the indication of systemic therapy vs locoregional therapy in hepatocellular carcinoma treatment. It appears based on the results and statistical analysis, one could infer that BCLC stage B and stage C patients were included. However, systemic therapy was recommended in stage C, not stage B in the original BCLC classification. It is scientifically sound (and clinically beneficial) to go beyond the guidelines. However, the authors should explain the rationale of rendering lenvatinib to BCLC stage B patients. Was it due to tumor progression? The authors mentioned that the diagnosis of HCC was based on either histological evidence or radiographic evidence. What was the percentage of either method? Did some patients have both histological evidence and radiographic evidence of HCC? Among those who had received biopsy, what was the histological grade distribution (poorly differentiated, moderately differentiated, vs well differentiated, etc.)? What radiographic classification was used? The study period which ended in December 2019



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
<https://www.wjgnet.com>

was recent enough for the authors to go back and re-examine these questions. One issue in the monitoring tumor response is the use of imaging. The author mentioned that RECIST 1.1 was used, which was published in 2009. Perhaps the authors should consider the addition of more up-to-date imaging criteria such as LI-RADS 2018. One question regarding the analysis of the results is the presence of hepatitis B infection. Does it make a difference in the treatment response vs those without hep B? It is unclear if the authors thought about this question regarding the highly prevalent viral infection among the Chinese population.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 55265

Title: Efficacy and Safety of Lenvatinib for Patients with Advanced Hepatocellular Carcinoma: A Novel Real-World Study Conducted in China

Reviewer's code: 04737401

Position: Peer Reviewer

Academic degree: MD

Professional title: Assistant Professor

Reviewer's Country/Territory: Egypt

Author's Country/Territory: China

Manuscript submission date: 2020-03-14

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-03-15 07:54

Reviewer performed review: 2020-03-25 09:37

Review time: 10 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

SPECIFIC COMMENTS TO AUTHORS

The idea is very excellent and manuscript had language editing and there are some grammar mistakes. The list of abbreviation not found and some abbreviations not found as DCR, AEs,PFS,RFA,ECOG-PS scores,MVI and EHS,FGFRs, VEGF and FGF
Methods: ECOG-PS score, ALBI stage, Child-Pugh class and BCLC stage needs references and hcv patients you should how to diagnose and what investigations you made for the undiagnosed cases as regards results (diarrhea in two patients) was written by mistake Base line AFP is NOT mentioned and follow up level should be mentioned and what about the cases with normal AFP Discussion: the first paragraph is mentioned previously in the result . you should focus on discussion only

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 55265

Title: Efficacy and Safety of Lenvatinib for Patients with Advanced Hepatocellular Carcinoma: A Novel Real-World Study Conducted in China

Reviewer's code: 00160160

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2020-03-14

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-03-15 23:34

Reviewer performed review: 2020-03-26 12:54

Review time: 10 Days and 13 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors reported the efficacy and safety of lenvatinib for patients with advanced hepatocellular carcinoma in China. However, there are several criticisms for publication. Detail comments are listed below.

Major

#1 Title, 1-1 The author decided the title of this study 'Efficacy and Safety of Lenvatinib for Patients with Advanced Hepatocellular Carcinoma: A Novel Real-World Study Conducted in China'. This study was a single-center, small number, and retrospective study. So, this title is exaggerated to mention a real-world clinical study in China, especially from the point of view in the effect of lenvatinib treatment for HBV related HCC patients.

#2 Result, 2-1 The author mentioned therapeutic response predictions based on AFP and gene mutation. But, this paper does not show the profile of AFP in the enrolled patient. Please show the detailed data.

#3 Discussion, 3-1 The author mentioned therapeutic response predictions based on AFP and gene mutation. Please show your opinion based on the relationship between tumor shrinkage and gene mutation, especially.

Minor

#1 Method 1-1 Abbreviation 2.3 Further analysis of baseline characteristics ECOG-PS, BCLC 1-2 Spelling miss 3.2 Assessment of efficacy and AEs during the entire treatment period ALBI grade I...1, II...2, III...3 palmar-plantar erythrodysesthesia by diarrhea in two patients

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 55265

Title: Efficacy and Safety of Lenvatinib for Patients with Advanced Hepatocellular Carcinoma: A Novel Real-World Study Conducted in China

Reviewer's code: 05246416

Position: Peer Reviewer

Academic degree: MD

Professional title: Assistant Professor, Attending Doctor

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2020-03-14

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2020-05-12 22:53

Reviewer performed review: 2020-05-12 23:41

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgooffice@wjgnet.com
<https://www.wjgnet.com>

The authors have taken much care in responding to the reviewers' comments and revising their manuscript. Grammatical errors have been corrected. Usage and diction have been polished. However, I still think it's vitally important to mention certain key inclusion criteria in the manuscript (e.g., BCLC B and C, Child A and B), especially given that there is no work count limit. This should be easily taken care of by two to three sentences. Without mentioning the specifics, the phrase "strict eligibility criteria" sounds like a cliché. I agree that RECIST is superior than LIRADS 2018 in terms of the study purposes. Is there a reason why the authors elected to use RECIST 1.1 rather than mRECIST? In terms of the effect hepatitis B had on the treatment response, perhaps a simple chi square or Fisher exact test would do--a total sample size of 54 would suffice. Just by eyeballing their Table 3, there appears to be some differences, and it'd be interesting to find out if these would be statistically significant or not.