



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 48191

**Title:** HER2 heterogeneity is a poor prognosticator for HER2 positive gastric cancer

**Reviewer's code:** 03766000

**Reviewer's country:** China

**Science editor:** Ying Dou

**Reviewer accepted review:** 2019-04-19 02:40

**Reviewer performed review:** 2019-04-19 09:53

**Review time:** 7 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input checked="" type="checkbox"/> Grade D: Fair	<input checked="" type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

In this manuscript, Akio Kaito et al explored the clinical significance of intratumoral HER2 heterogeneity for HER2 positive gastric cancer which has received trastuzumab-based chemotherapy, and found that HER2 heterogeneity might be the pivotal predictor to trastuzumab-based chemotherapy. Major concerns: The results



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part of this manuscript is too simple and short. The total words of results part were 347 with 5 figures and 2 tables. The authors should logically describe every figures and tables with more details.      Minor concerns    1 The supplementary figure 1 was not depicted in the manuscript.    2 There are so many digraphs in the manuscript. They should be divided. For example, patientsthan (Line 2, Page 7), IHC 2+than (Line 2, Page 7).    3 Many grammar errors need to be corrected:    Line 3, Page 5: “XPT or FPT regimen were”, Line 7, Page 14: “those portion”, and so on.    4 The duplicated table title in Page 24 should be deleted.

#### INITIAL REVIEW OF THE MANUSCRIPT

##### *Google Search:*

- The same title
- Duplicate publication
- Plagiarism
- No

##### *BPG Search:*

- The same title
- Duplicate publication
- Plagiarism
- No



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 48191

**Title:** HER2 heterogeneity is a poor prognosticator for HER2 positive gastric cancer

**Reviewer's code:** 03270428

**Reviewer's country:** China

**Science editor:** Ying Dou

**Reviewer accepted review:** 2019-04-17 04:58

**Reviewer performed review:** 2019-04-22 11:00

**Review time:** 5 Days and 6 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input checked="" type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

The manuscript found: Intratumoral HER2 heterogeneity by IHC was a significant predictor of clinical response and a poor prognosticator for trastuzumab-based chemotherapy. The conclusions appropriately summarize the data that this study provided. And the result is interesting. It reminds that Intratumoral HER2 heterogeneity



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would be useful to further stratify patients with HER2 positive gastric cancer, and thus should be taken into account in future clinical trials. The manuscript is well written.

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##### *BPG Search:*

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- No



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 48191

**Title:** HER2 heterogeneity is a poor prognosticator for HER2 positive gastric cancer

**Reviewer's code:** 00068459

**Reviewer's country:** China

**Science editor:** Ying Dou

**Reviewer accepted review:** 2019-04-16 09:45

**Reviewer performed review:** 2019-04-30 08:01

**Review time:** 13 Days and 22 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

The aim of this study is to provide evidence for the clinical significance of intratumoral HER2 heterogeneity for HER2-positive gastric cancer patients receiving trastuzumab-based chemotherapy. The conclusion based on multiple-site biopsy specimen should be more solid than endoscopic biopsy specimen, and quite helpful for



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clinical management of those patients. One weakness of the work is the number of patients, that only 82 patients were included in the final evaluation of intratumoral HER2 heterogeneity, and only 20 were defined as hetero, which limits the reliability in further subgroup analysis. It will be good to include more patients after December, 2016 if possible. Also, please address more on possible explanations for the results in discussion section, i.e., why the overall response rate was significantly better in the patients without HER2 heterogeneity (Homo group), why the progression free survival of trastuzumab-based chemotherapy was significantly better in the Homo group, why the overall survival was also significantly better in the Homo group.

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