

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 45386

**Title:** Significance of HER2 protein expression and HER2 gene amplification in Colorectal Adenocarcinomas

**Reviewer's code:** 00600507

**Reviewer's country:** Denmark

**Science editor:** Ruo-Yu Ma

**Date sent for review:** 2018-12-26

**Date reviewed:** 2019-01-02

**Review time:** 7 Days

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 checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input checked="" 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 checked="" 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

General comments: Information on HER2 expression and HER2 amplification in CRC is limited and due to the large number of samples tested in your study the current paper is of interest. However, especially in relation to the discussion section your paper needs to

be improved. Specific comments: 1. Introduction Please mention that HER2 is a predictive factor for treatment with trastuzumab in both breast and gastric cancer. 2. Immunohistochemical analysis You state: "HER2 IHC scores of 2+ and 3+ were considered as being "HER2 positive", while IHC scores of 0 and 1+ were considered as being "HER2 negative". Please state that this is different compared to the scoring criteria for gastric cancer. Please see World J Gastroenterol 2014; 20(16): 4526-4535. Results Were there any differences observed between the colon cancer and the rectal cancer populations. Please describe. Discussion a. You state: "No tumors with HER2 IHC scores of 1+ showed evidence of HER2 gene amplification by FISH". Based on the analyses of only 10 samples with IHC1+ it is difficult to state this. For the TOGA trial (Lancet 2010; 376: 687-697) in gastric cancer a relatively large proportion of patients with IHC0 and IHC1+ score were FISH+. Please discuss this in relation to your study and moderate your statement of no evidence of HER2 amplification in the IHC1+ group. b. You state: "Our study also indicates that there is a high concordance between HER2 IHC 3+ staining and HER2 gene amplification in colorectal adenocarcinomas." For the IHC3+ population an agreement with FISH+ is expected to be in the range of 90-100%. Please explain that you only achieved an agreement of 83%. c. In relation to the discussion on the prognostic nature of HER2 positivity in CRC, please also discuss this in relation the information available for gastric cancer. Please see Int J Cancer 2012; 130: 2845-2856 and J Cancer 2012; 3: 137-144. d. You state that you found a high agreement between IHC and FISH, so please explain why you mainly only found a prognostic association for HER2 amplification and not for HER2 expression. e. Please discuss the differences observed between the colon cancer and the rectal cancer populations if any.

## INITIAL REVIEW OF THE MANUSCRIPT

*Google Search:*



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- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

***BPG Search:***

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

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**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 45386

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**Reviewer's code:** 03551828

**Reviewer's country:** Japan

**Science editor:** Ruo-Yu Ma

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			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

Please explain the meaning of the association between patient's age and HER2. What is the scientific background for the association? The authors need to consider tumor sidedness but not tumor site as a prognostic marker. It has been reported that there is



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significant difference in HER2 positivity between right colon vs. rectum [Oncotarget. 2017 Sep 21;8(49):86356-86368]. Please discuss the previous report regarding tumor biological difference according to tumor site [Clin Cancer Res. 2018 Mar 1;24(5):1062-1072].

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

##### ***BPG Search:***

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No