

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 15979

Title: High HER-2 protein levels correlate with clinico- pathological features in colorectal cancer

Reviewer's code: 00071764

Reviewer's country: United Kingdom

Science editor: Yuan Qi

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed 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 checked="" 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 checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This article represents a novel meta-analysis of Her-2 expression in colorectal adenocarcinoma. Explicit explanation of all of the CASP questions are not necessary, and could be omitted. Logical meta-analysis protocols have been followed, although some concern exists regarding the virtual unanimity of the results, as the authors themselves admit that this is a controversial area. You do not appear to have included references 11 & 12 within the statistical analysis. Indeed, you state that 30 publications are used for the analysis, but only 14 are included in the Forest plots. This disparity is not commented upon in the text. In study selection, there are 2 consecutive sentences stating that differing numbers of articles were excluded due to data integrity, 41 and 75 respectively. Is there a different reason behind exclusion of either group, or could this figure be combined? This is not clear. Statistical analysis seems sound within the selected papers. The forest plots in figure 3 are difficult to interpret as no reference has been made as to what represents either a case or a control. In their current state they suggest that Her-2 expression is favoured in controls, which is against what has been concluded from the data. Comments regarding publication bias are difficult to follow. If there

is publication bias in CRC patients as a whole as stated in the paper, then why has ongoing analysis been performed at all? It suggests a wider inclusion of papers with negative results is needed, which also fits with my earlier suggestion that the range of papers included seems rather biased in favour of positive results. The discussion is rather brief, and could be extended to comment upon the likely role for herceptin in adjuvant treatment of colorectal cancer. The conclusion that Her-2 expression is correlated with advanced disease is not justified, as there is no significant difference in expression when assessed by TNM stage, but just Dukes stage - I am unsure how this disparity exists as the entities are very similar. The reasons for this disparity needs to be commented upon. Do you for instance only mean the 'T' component of the TNM staging system? IHC is notoriously difficult to get right in new settings, and standardisation is not agreed. Also, what criteria for positivity of HER-2 expression was used in the publications - strong staining, or just some staining. Is comment made as to where within the tumour the staining is present? You mention using FISH, but there is no reference or reason for suggesting this - please expand. How do the authors account for the disparity in significance between 3 and 5-year DFS? Is Her-2 a marker of likely recurrence, and if so, why is this not observed at 5 years? Overall, the article needs polishing in terms of its written english as some phrases are difficult to understand which impacts on the readability of the paper.