



# BAISHIDENG PUBLISHING GROUP INC

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## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 25905

**Title:** Role of targeted therapy in metastatic colorectal cancer

**Reviewer's code:** 00503404

**Reviewer's country:** Hungary

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-03-26 18:14

**Date reviewed:** 2016-05-16 23:05

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> [ Y] Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> [ Y] 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"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> [ ] Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> [ Y] No	<input type="checkbox"/> [ ] Minor revision
		BPG Search:	<input type="checkbox"/> [ ] Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> [ Y] No	

### COMMENTS TO AUTHORS

A comprehensive, well written review paper



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## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 25905

**Title:** Role of targeted therapy in metastatic colorectal cancer

**Reviewer's code:** 00041966

**Reviewer's country:** Italy

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-03-26 18:14

**Date reviewed:** 2016-05-19 22:30

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input 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 checked="" type="checkbox"/> Plagiarism	<input checked="" 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 is a comprehensive review on the use of biologic in conjunction with cytotoxic drugs in metastatic colorectal cancer patients. The manuscript is nicely written and provides an overview of the current literature on the subject. In the tables summarizing the principal results of the reported studies it could be useful to report the regimen of both arms with significant differences.

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 25905

**Title:** Role of targeted therapy in metastatic colorectal cancer

**Reviewer's code:** 02849903

**Reviewer's country:** Japan

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-03-26 18:14

**Date reviewed:** 2016-03-27 01:15

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

### COMMENTS TO AUTHORS

In this review, Ohhara et al provide a clear summary of the role of targeted therapy in metastatic colorectal cancer. Overall, the text is clear and this review should be valuable for both World Journal of Gastroenterology readers not particularly familiar with targeted therapies and specialists in the field. My suggestions to further improve the quality of the paper are; Major: 1. According to the title of this review, it would be better to briefly summarize clinical studies of targeted therapy other than EGFR and VEGF (e.g. "A randomized, placebo-controlled phase 2 study of ganitumab or conatumumab in combination with FOLFIRI for second-line treatment of mutant KRAS metastatic colorectal cancer", Ann Oncol, 2013). 2. The paper by Hong et al ("A phase II study of bevacizumab, oxaliplatin, and capecitabine in patients with previously untreated metastatic colorectal cancer: a prospective, multicenter trial of the Korean Cancer Study Group", Am J Clin Oncol, 2014) should be included as reference. 3. As the authors mentioned, KRAS status is a well-described biomarker for the EGFR-targeted therapy. Although the survival of patients with wild type KRAS is better than with mutant KRAS, the tumor eventually relapse regardless of EGFR inhibition. Thus, it is really important to elucidate the mechanism of acquired resistance to targeted therapies. A seminal report



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in Nature (Diaz et al, "The molecular evolution of acquired resistance to targeted EGFR blockade in colorectal cancers", 2012) has shown that the emergence of mutant KRAS from wild type KRAS is a mediator of acquired resistance. I suggest the authors to include this paper in this review to strengthen the point that mutant KRAS is a valid biomarker in EGFR inhibitor treatment. 4. Most of the inhibitor, which are currently available in clinic, are antibody-based reagents. Santoro et al has shown that gefitinib (EGFR TKI) did not improve the efficacy of FOLFIRI in mCRC (Santoro et al, Ann Oncol, 2008). Is this because of the bioactivity of antibody such as ADCC and CDC? Minor: Typo in the title of Table 1.



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### ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 25905

**Title:** Role of targeted therapy in metastatic colorectal cancer

**Reviewer's code:** 00505466

**Reviewer's country:** Greece

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-03-26 18:14

**Date reviewed:** 2016-03-27 19:55

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
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		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

### COMMENTS TO AUTHORS

The authors provide a very comprehensive and extended overview of targeted therapy for metastatic colorectal cancer. It is a very long exhaustive) summation of data from clinical trials. A few comments are to be made. This manuscript seems to me more suitable for a (medical) oncology journal and not for a gastroenterology journal. I would like to ask the authors to discuss whether there are differences in outcome for colon versus rectal cancer metastases. In these days of economic crisis, the additional treatment costs for a survival benefit of a few months has to be discussed. Page 8. 'IFL' should be explained as 'irinotecan, fluorouracil, and leucovorin' at first appearance.