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Flat C, 23/F., Lucky Plaza,  
315-321 Lockhart Road,  
Wan Chai, Hong Kong, China

## ESPS Peer-review Report

**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 5778

**Title:** Sequencing of Treatment in Metastatic Colorectal Cancer: where to fit the target?

**Reviewer code:** 00181023

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-09-26 18:26

**Date reviewed:** 2013-10-07 16:00

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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 checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

The manuscript by Temraz and colleagues provides a well-balanced comprehensive overview on the different treatment options in patients with metastatic colorectal cancer. Overall, the manuscript is well written and need only minor language polishing. Some issues, should, however, be addressed which should result in significant amendment of the manuscript. 1. Introduction, line 1: There is no "lack of appropriate screening". There is screening colonoscopy and this is increasingly applied in many countries with good success. Please re-phrase this sentence. 2. Introduction, line 4: It should be made clear, that "metastatic disease" refers to distant metastasis, as locoregional lymph node metastasis is more common (and adjuvant therapy is not the topic of this review). 3. It should be made clear, if differences exist between colon and rectal cancers - if there are divergent data in the literature, these should be mentioned. If they do not exist, the reader should be informed that the presented data are valid for both types of cancer. 4. R0-resection rate: the term occurs at several occasions throughout the manuscript: At the first instance it should be made clear what you talk about, most probably the R0-status of resected hepatic metastases (and not the primary tumor). 5. Page 4: Please check throughout the manuscript: Sometime you write 5-FU (what I prefer) and sometimes FU alone - there should be one wording throughout the manuscript. 6. Page 6 beginning of "Cetuximab versus bevacizumab": There is "AIO" not explained, but explain that on page 10 (bottom). It should, however, be explained already on page 6. Please write "Arbeitsgemeinschaft Internistische Onkologie" in three separate words. 7. Page 9, lines 2-3 (and again page 12, three lines from the bottom): Are you sure that "wild-type KRAS exon 2, but mutated other RAS (KRAS exons 2,3 or..." is correct? In my opinion this is a contradiction. 8. Page 14, line 4. The statement regarding BRAF is an over-simplification, if not entirely wrong: MSI-H tumors with BRAF mutation have a



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good prognosis, the bad guys are the BRAF-mutated microsatellite stable (MSS) tumors (please compare Bettington et al. *Histopathology*, for review). Thus, please re-phrase this sentence. 9. Page 14, last sentence of the second paragraph: Please change “shall” into “can” (or “could”). 10. Page 17, two lines from the bottom - to stay in the style of comparable sentences please write “ECOG (Eastern Cooperative Oncology Group) study E3200”. 11. Finally, I agree that “no supportive funding” is okay for a review, but “conflicts of interest” should nevertheless be mentioned for a review like this (even if they are not there).



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## ESPS Peer-review Report

**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 5778

**Title:** Sequencing of Treatment in Metastatic Colorectal Cancer: where to fit the target?

**Reviewer code:** 00646241

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-09-26 18:26

**Date reviewed:** 2013-11-12 05:38

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

In their work, "Sequencing of Treatment in Metastatic Colorectal Cancer: where to fit the target?", Temraz S et al., the authors give a very detailed and diligently written overview of the published data on systemic therapy in metastatic colorectal cancer, with particular focus on targeted drugs given in addition to standard cytostatics. The paper is well written and full of details. I am not aware of any detail or study missing. In the discussion, the collected data are interpreted carefully, and the conclusions drawn are convincing. In their conclusion, the authors sketch new models of studies based on treatment sequences including line one and subsequent treatment lines. Probably, such modes of clinical studies will be of extreme benefit in the future, with numerous targeted therapies coming up in an era of individualised therapy of cancers that are characterised by new molecular genetic methods. Thus the paper contributes significantly to future strategy planning. The literature references are impressive. The figure is clear and evident from the text. One minor typing error: p.19: instead of 5-FU or capecitabine is a weak regimen limited to better write 5-FU or capecitabine is a weak regimen limited to