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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 8124
Title: Rationally designed treatment for metastatic colorectal cancer (mCRC): current drug development strategies.
Reviewer code: 00040410
Science editor: Zhai, Huan-Huan
Date sent for review: 2013-12-18 11:09
Date reviewed: 2013-12-31 13:37

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
The manuscript needs some minor revisions (see notes attached). One of the scopes of the review is to identify responders (sentence highlighted by me in yellow in the abstract). In this the manuscript is not very helpful. More papers such as the ones of De Rook et al. Lancet Oncology (reference 11) should be reviewed to achieve this goal. Otherwise the sentence can be taken out of the abstract. However, the review would be much more helpful if it highlight the subset of patients with metastatic colorectal cancer in whom these very expensive drugs could give a survival benefit. My minor comments are found in the copy attached.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 8124
Title: Rationally designed treatment for metastatic colorectal cancer (mCRC): current drug development strategies.
Reviewer code: 00002971
Science editor: Zhai, Huan-Huan
Date sent for review: 2013-12-18 11:09
Date reviewed: 2014-01-03 15:48

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[Y] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
This invited review gives an excellent and succinct summary of new treatments for metastatic colorectal cancer. There are few specific issues which need attention: - it is mentioned that the disease is invariably fatal and the only treatment is chemotherapy. It should be briefly acknowledged that a small number of patients can be successfully treated by surgical resection of iver metastases - in 2 places on page 3, approval for use of agents is mentioned. Presumably the approval referred to is in the United Kingdom. It is not the same in my country for example. Since this article is for an international audience, the reference to specific approval should be deleted. - the section related to microsatellite instability is inaccurate. Inactivation of MLH1 protein does not lead to BRAF mutation. The BRAF mutation is present in the benign colorectal polyp from which the cancer arises. The tendency of these tumours to acquire heavy CpG island methylation (CIMP) leads to methylation and silencing of MLH1 at the time the benign polyp transtions to invasive malignancy. CIMP should be mentioned as background to the discussion to DNA-methylating agents. Also sundromes should not be plural at the top of page 8. There is only one relevant syndrome (Lynch syndrome) -the tables should be referenced in the text - the section headings (Mitogen-activated protein kinase (MAPK) pathway, PI3K-AKT-mTOR pathway etc) should be made clearer with different font - on page 5, line 6 "where" should be "were"

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 8124
Title: Rationally designed treatment for metastatic colorectal cancer (mCRC): current drug development strategies.
Reviewer code: 02533933
Science editor: Zhai, Huan-Huan
Date sent for review: 2013-12-18 11:09
Date reviewed: 2014-01-10 08:57

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[Y] Accept
[Y] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS
Dr. Spiliopoulou and Dr. Arkenau have submitted a review titled "Rationally designed treatment for metastatic colorectal cancer: current drug development strategies". In that review-paper the authors summarized current attempts to improve treatment results using molecular targeted agents in colorectal cancer and their rational. I have only one suggestion. The target of that kind of paper are clinicians and some of them might not be completely familiar with the molecular pathways and interconnections between them, so to make the paper more complete and understandable, I would recommend to add 1 or 2 schemes showing the molecular pathways in a cell context including the names of the drugs described in this manuscript.