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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology
ESPS manuscript NO: 26745
Title: Oncogenic fingerprint of epidermal growth factor receptor pathway and emerging epidermal growth factor receptor blockade resistance in colorectal cancer
Reviewer's code: 00477066
Reviewer's country: Italy
Science editor: Fang-Fang Ji
Date sent for review: 2016-04-26 14:05
Date reviewed: 2016-05-04 04:12

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

COMMENTS TO AUTHORS

This is a well written review. Future perspectives should be better described.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology
ESPS manuscript NO: 26745
Title: Oncogenic fingerprint of epidermal growth factor receptor pathway and emerging epidermal growth factor receptor blockade resistance in colorectal cancer
Reviewer's code: 02148395
Reviewer's country: Germany
Science editor: Fang-Fang Ji
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The review "Oncogenic fingerprint of EGFR pathway and emerging EGFR blockade resistance in colorectal cancer" by Zain A Sobani et al. is concerned with anti-EGFR resistance in colorectal cancer with KRAS, BRAF, PIK3CA or PTAN mutations. The authors suggest that alterations in the EGFR pathway might have an impact on anti-EGFR resistance in KRAS wt patients, a subject that warrants further studies. The short introduction provides the essential information for starting the first chapter on the oncogenic signature of EGFR pathway, with signaling activating several prosurvival pathways. In cancer cells the initial trigger via EGFR is not required for KRAS activation. P13K is another pathway that may become independent of the EGFR. The authors next introduce BRAF, src and STAT. In the following the authors focus on chimeric anti-EGFR antibodies as therapeutic strategy, which promote internalization and can inhibit RTK activity. It follows a somewhat lengthy description of clinical trials that may benefit from some shortening. Building on early signs of emerging resistance the authors proceed with studies concerned with the underlying mechanisms. One of the prime reasons are KRAS mutations, followed possibly by BRAF. A contribution of loss of

Pten and increased MET activity also require further confirmation. This section is merely descriptive and does not add information beyond that in the chapter on the oncogenic signature. In the last chapter the authors focus on the mechanisms underlying therapy resistance in wild type KRAS patients. They report on studies describing emergence of mutations or outgrowth of distinct clones or introduction of resistance by distinct RTK pathways. The main message of the conclusion is the requirement of studies elaborating genomic alterations during antibody therapy. References would benefit from being updated. Few citations are included beyond 2012. In brief, as the review remains mostly on the level of listing results of clinical studies being very descriptive, I suggest that it will be interesting mostly for clinicians considering optimal patients' treatment. Taking this into account, a considerably shortened version will be more attractive.