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PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 38246

Title: FOLFIRI3-aflibercept as second or later-line therapy in patients with metastatic colorectal cancer

Reviewer's code: 02977366

Reviewer's country: China

Science editor: Fang-Fang Ji

Date sent for review: 2018-04-11

Date reviewed: 2018-04-16

Review time: 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[Y] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [Y] Advanced [ ] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

There is one question for the authors: Is there a dose finding stage for FOLFIRI3-aflibercept regime? What is the basis for determining the dosage of this regime?

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PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 38246

Title: FOLFIRI3-aflibercept as second or later-line therapy in patients with metastatic colorectal cancer

Reviewer's code: 02521495

Reviewer's country: Slovenia

Science editor: Fang-Fang Ji

Date sent for review: 2018-04-11

Date reviewed: 2018-04-19

Review time: 8 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [ ] Advanced [Y] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This is a retrospective, small sample size study using modofied chemotherapy+ targeted therapy in patients with metastatic CRC. The results are promising, indicating that the combination is effective in irinotecan naive and pre-treated patients. The manuscript is

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well written ,the english is good and no corrections are needed. The tabels, graphs are clear, the literature is cited well. The statistics is appropriate. I agree with authors tha t randomised trial on bigger sample size would be the next step.

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PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 38246

Title: FOLFIRI3-aflibercept as second or later-line therapy in patients with metastatic colorectal cancer

Reviewer's code: 03017141

Reviewer's country: Japan

Science editor: Fang-Fang Ji

Date sent for review: 2018-04-11

Date reviewed: 2018-04-22

Review time: 11 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [Y] Advanced [ ] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This is unique study evaluation the efficacy and safety of FOLFIRI3 plus aflibercept in ordinal clinical setting, that may encourage future prospective trial with the relatively high response rate. However, there are some points authors may re-consider. #1.

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Authors should provide the reasons for discontinuation of the prior irinotecan treatment in irinotecan pre-exposed population. Authors cannot conclude FOLFIRI3＋aflibercept is promising for irinotecan pre-exposed patients if those patients were not refractory to irinotecan. #2. There were too many toxicity related discontinuation of therapy (46.7%) despite dose reductions in this study. In VELOUR study, the proportion of adverse event related discontinuation was 26.8%. This may be attributed to specific UGT1A1 genotype, namely *28/*28, which leads to higher incidence of serious toxicity with irinotecan. Can author reveal the patients UGT1A1 status? #3. Can authors provide detailed profile of prior treatment in both groups? In VELOUR sub-group study (Chau, et al. BMC Cancer 2014), they suggested adjuvant fast relapse is a favorable predictive factor for FOLFIRI plus aflibercept.

INITIAL REVIEW OF THE MANUSCRIPT

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