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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 28636

Title: Efficacy of Olaparib in colorectal cancer patients with alteration in homologous repair protein.

Reviewer's code: 01441415

Reviewer's country: Japan

Science editor: Ze-Mao Gong

Date sent for review: 2016-07-11 18:14

Date reviewed: 2016-07-26 13:05

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|---------------------------------------------------|-----------------------------------------------------------------------|------------------------------------------------|--------------------------------------------------------|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input type="checkbox"/> Grade B: Very good | <input checked="" type="checkbox"/> 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"/> 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 type="checkbox"/> Plagiarism | <input type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E: Poor | | <input checked="" type="checkbox"/> No | <input checked="" type="checkbox"/> Major revision |
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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

This manuscript by Ghiringhelli et al. et al. reported two cases of metastatic colorectal cancer (CRC) patients who treated with relatively new molecular targeted agent, PARP inhibitor (olaparib), and one of two patient had a good response of tumor. Authors concluded that olaparib may have efficacy in CRC patient with homologous repair deficiency. Although the treatment experience by olaparib is less novel, because Phase II trial of olaparib in CRC has already reported (Leichman L, et al. Oncologist 2016), the therapeutic concept of exome analysis-guided selection of molecular targeted agent has a considerable potential of future treatment strategy. This manuscript is written in acceptable language quality and well-written discussion. Authors are recommended to incorporate the past knowledge and future perspectives regarding combination therapy with olaparib, such as irinotecan.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 28636

Title: Efficacy of Olaparib in colorectal cancer patients with alteration in homologous repair protein.

Reviewer's code: 00057695

Reviewer's country: Saudi Arabia

Science editor: Ze-Mao Gong

Date sent for review: 2016-07-11 18:14

Date reviewed: 2016-08-16 12:20

| 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"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Duplicate publication | <input type="checkbox"/> Rejection |
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| <input type="checkbox"/> Grade E: Poor | | <input type="checkbox"/> No | <input type="checkbox"/> Major revision |
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| | | <input type="checkbox"/> No | |

COMMENTS TO AUTHORS

This case report highlighting the importance of the exome sequencing analysis before administering targeted therapy. However, the most challenging issue of using exome sequencing for the purpose of cancer-causing variant detection is analyzing and filtering the large number of detected variants. This needs to be highlighted in the discussion. Also, the use of targeted therapy such as poly ADP ribose polymerase (PARP) inhibitor therapy such as olaparib 400 mg p.o. b.i.d, in patients with colorectal cancer and inefficient tumor DNA repair mechanisms, such as those with microsatellite instability (MSI-H) has been studied in a phase II study. It was found that single-agent olaparib delivered after failure of standard systemic therapy did not demonstrate activity for CRC patients, regardless of microsatellite status (Leichman L, et al. Oncologist. 2016). Unfortunately, such trial was not alluded to in the discussion. Also, another recent Phase 1 study (Chen EX, et al. Invest New Drugs. 2016) was conducted to evaluate the safety and tolerability of olaparib, but in combination with irinotecan in patients with advanced colorectal cancer whose disease progressed after at least one systemic therapy regimen. Again, this study was not referred to in the discussion. Other comments: 1. Indicate the



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dose of olaparib given to both patients. 2. Although, the drug worked for Case 1, albeit for a short period of time, its use failed in case 2. 3. What is the cost of conducting the exome analysis? Also indicate the cost of olaparil course and the expected side-effects. 4. The language needs polishing in certain areas of the "Case Report: patient 1 and patient 2). Also, in the discussion.