



PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 54721

Title: Acute myelomonocytic leukemia during pembrolizumab treatment for non-small cell lung cancer: A case report

Reviewer's code: 02453616

Position: Peer Reviewer

Academic degree: PhD

Professional title: Director, Doctor

Reviewer's Country/Territory: United States

Author's Country/Territory: South Korea

Manuscript submission date: 2020-02-14

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2020-04-25 21:49

Reviewer performed review: 2020-05-07 01:44

Review time: 11 Days and 3 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

The authors reported a case of squamous NSCLC treated with platinum doublet with PR for 12 weeks and then PD per RECIST. Subsequent pembro treatment for 9 weeks led to CR, but quickly was discontinued due to SAE. Unfortunately, the patient presented URT infection and increased WBC count, and was then diagnosed having AML. The pulmonary complications and fast clinical deterioration of this patient are consistent with a subset of AML patients who have hyperleukocytosis defined by $>100K/\mu L$ WBC counts. The origin of the AML is still unknown, given the clinical evidence described here without any molecular characterization of the malignancies from both the NSCLC and AML. The authors believe that this is an AE related to pembro treatment. However, I don't think the evidence presented here is strong enough to either prove or disapprove this, nor could they prove or disapprove any other possibilities. Most critically, as the authors pointed out themselves, "among the adverse events observed with pembrolizumab treatment, acute myeloid leukemia (AML) has not been reported", isn't it true that extra caution needs to be taken when they tried to build this case without published precedence? This is the burden and responsibility the authors need to bear. I suggest two possible paths for this manuscript. One is to provide stronger evidence to support the possibility that the AML is pembro-related, or they should tone down the whole manuscript about the relationship between AML and the pembro treatment, and balance it by discussing other possibilities in more details. They did discuss briefly two other possibilities, one of being related to prior doublet treatment. The other one is that the AML is a separate malignancy that grew out of a pre-clinical scale into hyperprogression after pembro. Metachronous or synchronous presentation of AML and lung cancer was already well-documented. However, defining the current clinical course as hyperprogression is quite questionable for two reasons. First, most documented



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hyperprogression describes a longitudinal evolution of a malignancy, particularly there are tumor assessments before AND after the immunotherapy, so the dynamics of the progression can be clearly defined. In this case, there is no assessment of the AML before pembro, so how can the authors be sure this is not the natural course of the malignancy? Secondly, if there are prior documented cases of AML that became hypogressive after immunotherapy, please describe it as a supporting evidence. If there was no such prior case, then the likelihood would be small. Additional questions to the manuscript: 1. Is this patient a current or past smoker? If yes, please document the smoking history and habit. Smoking is associated with both AML and squamous NSCLC. 2. Was there any cytogenetic and/or molecular analysis being performed in addition to the karyotyping? AML with normal karyotyping is not that unusual. AML with hyperleukocytosis and normal karyotypes was also documented before. How about the SQ NSCLC biopsy that was taken? Any analysis being done on that biopsy? 3. If the panels C and D in the Figure 2 have the same magnification as A and B, please specify. I can see where the panel B is inside the panel A, but for clarity to the readers, please either demarcate the panels A and C, or at least describe it clearly. 4. Figure 4 legend, is “hypogranuleation” a typo? 5. The headers of Table 1 are unclear. Please describe what Pem #1, #2, and #3 are in the legend. HD is hospital day, but is it possible to describe the relationship between the “Pem” days and the HD, for example, how many days away from the Pem#3? Please also include the reference (normal) values for each test for clarity to the readers. 6. For describing PD-L1 IHC staining result, please use the exact terms in the interpretation manual approved for 22C3 in NSCLC by Agilent, the TPS system.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Reviewer's Country/Territory: United States

Author's Country/Territory: South Korea

Manuscript submission date: 2020-02-14

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2020-05-30 01:37

Reviewer performed review: 2020-06-07 21:46

Review time: 8 Days and 20 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS



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The revision submitted by the authors is satisfactory, so accepting for publication is recommended.