Author's response to reviews

Title: Low rate of mutation and modest effect of SF3B1, U2AF1, and SRSF2 on prognosis in the myelodysplastic syndrome without ring sideroblasts

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Author’s response to reviews: see over
Dear Editor,

We are electronically submitting our revised manuscript for research article, “Low rate of mutation and modest effect of SF3B1, U2AF1, and SRSF2 on prognosis in the myelodysplastic syndrome without ring sideroblasts”, which we hope will be of interest to BMC Cancer and its readers.

Mutations in the genes of the splicing machinery have been studied recently in myelodysplastic syndromes (MDSs). However, to date, there is scarcity of informative studies examining splicing gene mutations in MDS without ring sideroblasts (RS). In this study, we examined a cohort of 129 de novo MDSs that did not harbor RS, for mutations affecting 3 splicesomal genes (SF3B1, U2AF1, and SRSF2).

Our key findings of the current study were as follows:

1) Compared to the previous study, these splicing gene mutations in MDS without RS were relatively infrequent: The mutation rates of SF3B1, U2AF1, and SRSF2 gene were 8.3%, 7.6%, and 9.8%, respectively.

2) The SRSF2 mutation was closely correlated with older age (P < 0.001). Meanwhile, the SF3B1 mutation status did not affect overall survival (OS), progression free survival (PFS), and AML transformation.

3) In contrast, patients with U2AF1 or SRSF2 mutation had an inferior PFS in all MDS patients as well as subgroups of MDS. In addition, the U2AF1 mutation was associated with inferior OS in higher risk MDS patients (P = 0.003). Interestingly, the SRSF2 mutation was associated with AML transformation (P = 0.048).

4) In conclusion, our findings suggest that the frequencies of the SF3B1, U2AF1, and SRSF2 splicing gene mutations in MDS without RS were relatively low, and we demonstrate that the U2AF1 and SRSF2 mutations, unlike SF3B1, were associated with an unfavorable prognostic impact in MDS patients who do not harbor RS.

The following descriptions are point-by-point description of the changes according to editor’s comments or request.

EDITOR’S COMMENTS:
"Please clarify in the Methods section whether the mutation analysis described in the study was part of standard care. If not, please clarify whether written informed consent was obtained from the patients for the use of their sample in research”

We clarified in the Methods section whether written informed consent was obtained from the patients.
(page 7, Line 150~152)

EDITORIAL REQUEST:
1). Please remove authors information after Authors Contribution.
-> We removed authors’ information.

2). Please format figures.
-> We formatted figures depending on the instructions for authors.
This original research has not been previously published and has not been submitted for publication elsewhere while under consideration. All the authors have read and approved the work. The authors declare no conflict of interest. Thank you in advance for your careful consideration of our work.

Sincerely yours,

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