Author's response to reviews

Title: Tumour biology, metastatic sites and taxanes sensitivity as determinants of eribulin mesylate efficacy in breast cancer: results from the ERIBEX retrospective, international, multicenter study

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

Thank you very much for the attention, the useful comments and the interest manifested by Dr Anna Tessari, Dr Junji Tsurutani and yourself to our manuscript 9144236651605846 entitled “Tumour biology, metastatic sites and taxanes sensitivity as determinants of eribulin mesylate efficacy in breast cancer: results from the ERIBEX retrospective, international, multicenter study” submitted for publication as a Research Article in BMC Cancer.

We were happy to answer the reviewers’ comments which were useful and relevant. Our manuscript is now improved as we have modified it accordingly. You will find enclosed the reviewers’ report followed by a point-by-point answer to the requested revisions. In addition, the manuscript was copyedited by a native English speaker in order to improve the style of written English.

We hope that these modifications will allow the publication of our revised manuscript in BMC Cancer.

Sincerely yours,

On behalf of the authors,

William Jacot, MD, PhD
Response to Reviewers

Reviewer: Anna Tessari

Reviewer's report: This article reports the results from ERIBEX study, a retrospective, international, multi-center study aimed to evaluate the efficacy and safety of eribulin mesylate (EM) in metastatic breast cancer patients in daily clinical practice.

Due to the novelty of the drug, few data are available regarding clinical applications of EM outside clinical trials, so it is interesting to evaluate them in a routine setting. Authors performed a detailed analysis of EM efficacy, toxicity and pattern of response in terms of biological characteristics of the disease, metastatic spreading and previous treatments.

For these reasons I find it worthy of publication, with only minor considerations:

1- Figures and tables should be better labeled and the content of the items should be better clarified. Table 2 and 3 might be aggregated in a single table.

Thank you for this comment, the reviewer is right. We modified the Table and Figure labels and combined Tables 2 and 3 in Revised Table 2.

2- Some statements should be better clarified. For example, in line 285, rephrase the content in parenthesis. Please rephrase also the statement in line 290-292.

Considering line 285, we propose to rephrase as follow: “The most common cause of treatment discontinuation was disease progression (75%), followed by toxicity (13.1%), and patient's death (8.1%) ; also, 7.2% of the patients discontinued EM treatment due to other causes such as patient's or medical decision.”

Regarding the sentence in lines 290-292, we propose the following text: “Death was mainly related to disease progression (PD, 95.1%). Toxic death was reported in 2 cases (1.4%) and was related to intercurrent diseases in 5 cases (3.5%)."
Reviewer: Junji Tsurutani

Reviewer's report: Dell'Ova et al reported several clinicopathological variables as prognostic and predictive values in a multicenter-retrospective study on patients with advanced breast cancer treated with eribulin, but there exists limitation of interpretation on predictive value due to lack of comparison with no eribulin use. So, three factors they found are clearly prognostic in the study population, but not prognostic.

Minor points are as follows.
1. Line 99, reference 3 does not correspond to what authors describe here.
   The reviewer is right. This error has been corrected in the manuscript, and an appropriate reference has been inserted.

2. From line 173 to 176, what is "cure"? Also, even if patients with one cycle of treatment, they should be incorporated in the analysis. Otherwise, the study suffers selection bias.
   The word “cure” was not well chosen. We have replaced it by the word “injection” in the text.
   Also, very few patients (<5% of patients treated in the participating institutions) were vacationers, present for a short duration (< 1 month) of time during their holidays and began then pursued their EM treatment in their original hospital. As a comprehensive retrieval of their clinical and pathological data could not be performed, we decided not to include these patients in the present study. We do not think it could be a significant bias, but would have led to substantial loss of information due to incomplete data.

3. Line 210 and 211, what is "cure"?
   Again, the word “cure” may have not been well chosen. It has been replaced by the word “treatment” in the text.

Thank you for these useful comments.