Author's response to reviews

Title: Retrospective exploratory analysis of VEGF polymorphisms in the prediction of benefit from first-line FOLFIRI plus bevacizumab in metastatic colorectal cancer

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

we are pleased to transfer the submission of our manuscript titled “Retrospective exploratory analysis of VEGF polymorphisms in the prediction of benefit from first-line FOLFIRI plus bevacizumab in metastatic colorectal cancer” from Translational Journal of Medicine to BMC Cancer as “Research Article”.

The manuscript reports our original research experience evaluating the role of candidate VEGF gene polymorphisms in the prediction of benefit from first-line treatment of metastatic colorectal cancer patients with FOLFIRI plus bevacizumab. The monoclonal antibody bevacizumab is currently approved in many countries worldwide for the treatment of metastatic colorectal cancer in combination with fluoropyrimidine-based chemotherapy. At present, despite several attempts, no promising molecular marker of outcome has yet been found. The identification of predictors of bevacizumab activity and/or efficacy is a crucial key-point for translational research in colorectal cancer. This is especially true for those patients bearing KRAS wild-type tumours that are now candidate to receive bevacizumab or the anti-EGFR, cetuximab in combination with chemotherapy for the up-front treatment of their disease. So far, there are no data with regard to which antibody is better since direct comparisons are still ongoing. From this, derives that the choice of the optimal “biological partner” for chemotherapy is currently based on the personal experience of treating physicians. Therefore, the molecular selection of a subgroup with different chances of benefiting from bevacizumab may have relevant clinical implications/ reflections.

Our study, including 111 patients treated with FOLFIRI plus bevacizumab and a matched series of 107 historical controls treated with FOLFIRI-only, suggests for the first time that VEGF -1498 C/T allelic variants may influence the efficacy of bevacizumab. We do recognize that this is a non-randomized comparison and this may led to some criticisms. Nevertheless in our opinion, this could be considered as a strengthening point since the vast majority of published and ongoing experiences in the field of genetic profiling of cancer for pharmaco-predictive purposes are single-arm retrospective studies without any direct or indirect calibrative comparisons.

This report has not been previously published and it is not under consideration for publication elsewhere. No revisions have been made since the original submission. All named authors have agreed to its submission and declare no conflict of interest.

Thank you for your kind consideration of our manuscript.

Sincerely, on behalf of the authors,

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