Author's response to reviews

Title: Effect and safety of dual anti-HER2 therapy compared to monotherapy in patients with HER2-positive breast cancer: A Systematic Review and Meta-analysis

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Dear Editors,

With this letter we are submitting the enclosed manuscript entitled “Effect and safety of dual anti-HER2 therapy compared to monotherapy in patients with HER2-positive breast cancer: A Systematic Review and Meta-analysis” to BMC Cancer.

Breast cancer is a significant public health concern with more than a million new cases diagnosed annually, resulting in 400,000 deaths worldwide. The approval of trastuzumab, lapatinib and pertuzumab by FDA has changed the natural history of HER2-positive breast cancer. Despite all of these improvements, resistance to these agents remains a therapeutic challenge. One strategy is combining different HER2-targeted agents. Recently, many clinical trials have been conducted in dual anti-HER2 therapy compared with monotherapy. However, the frequency of AE has aroused some safety concerns. Furthermore, the need to adding chemotherapy and the component of dual agents also confused the clinicians. Hence, this meta-analysis provides a comprehensive summary of all the data currently available, and confirms the benefits and risks of dual anti-HER2 therapy for HER2-positive breast cancer.

Dual anti-HER2 therapy demonstrated significant benefits both in pCR (RR, 1.56; 95% CI, 1.23-1.97; p<0.001), PFS (HR, 0.71; 95% CI, 0.62-0.81; p<0.001) and OS (HR, 0.68; 95% CI, 0.57-0.82; p<0.001). Subgroup analyses showed that the addition of chemotherapy to dual anti-HER2 therapy may greatly improve pCR in the neoadjuvant settings. However, in the metastatic settings, similar significant benefits in PFS and OS were found in patients receiving dual anti-HER2 therapy with or without chemotherapy. Dual anti-HER2 therapy was associated with more frequent adverse events, however, no statistical differences were observed in cardiac toxicities.
No part of this paper has been published or submitted elsewhere. No conflict of interest exists in the submission of this manuscript. All of the authors agreed with the submission of the article.

Thank you very much.

Sincerely yours,

Jia He