

As suggested by reviewer 1, we have amended the authors name in the reference list such that all authors for each cited study are now visible.

We have already summarized the relevant literature comprehensively by supporting statements with evidence. As an example, we provided comprehensive explanation on why greater gut microbiome diversity is associated with better therapeutic response - "Study results showing associations with GM diversity were consistent with previous studies which showed that greater GM diversity is prevalent in healthy state across multiple diseases, plausibly suggesting that a greater GM diversity produces the optimal immune environment needed for normal physiological functioning(40-42). One major reason is the promotion of a favorable immune phenotype, as evidenced by the positive correlation between Shannon diversity index and several CD8+ T cell and NK cell signatures, required to produce a robust anti-tumoral response(38)". Furthermore, we included a comprehensive explanation as to why certain species are associated with better response to immunotherapy. As we described, "Previous studies have demonstrated that GM from Firmicutes family and Bacteroidales order play a significant role in mediating the response to immunotherapy in melanoma patients(12, 27, 29). For instance, abundance of Firmicutes was associated with increased frequencies of CD4+, CD8+ T cells, CD 45+ myeloid and lymphoid tumor-infiltrating cells and preserved cytokine response to anti-PD-1 therapy(12). Additionally, abundance of Firmicutes was linked with decreased frequency of intestinal and systemic regulatory T cells (Tregs) and B7+ T cells, cells responsible for limiting immune response robustness(27). This resulted in increased antigen presentation and effector T cell function in both the periphery and tumor microenvironment(12, 27, 29). However, other GM such as Bacteroidales were unfavorable in terms of anti-tumoral response in that its abundance was associated with higher frequencies of Tregs and myeloid-derived suppressor cells and a blunted cytokine response(12). These findings combined demonstrated that certain GM play a crucial role in mediating systemic and antitumor immune responses which have clear implications on efficacy on ICB therapy in metastatic melanoma patients.

Lastly, we have adjusted paragraph formatting and corrected spelling and grammatical errors as suggested by reviewer 1.

Reviewer 2's feedback of our manuscript was very good and had no comments to be addressed.

We have also attached a PRISMA checklist for your reference.

We have addressed all the feedback and comments given by reviewer 1 and 2 and believe that our manuscript is of high quality for publication in World Journal of Clinical Oncology.

Many thanks for your consideration of our manuscript.

Best wishes,

Dr Oliver Oey, MD on behalf of all authors