Reply to Shao and Zhou

We appreciate the comment by Shao and Zhou[1] regarding our recent meta-analysis on antibody response after vaccination against SARS-CoV-2 in adults with hematological malignancies.[2]

We agree with the authors that literature searches for reviews and meta-analysis are essential and using as many databases (commercial and public) as possible ensures accuracy. However, especially this unforeseen and unique evolution of scientific literature production during the COVID-19 pandemic poses extreme challenges for evidence synthesis in general. Therefore, we specifically decided to use publicly available databases for literature storage to enable the replication of findings for all stakeholders and make science more tangible. In that respect, we limited our study inclusion criteria to studies published in English language, original reports (excluding conference abstracts and comments), and reporting outcomes of at least ten patients in the overall reported cohort. Importantly, other co-published meta-analyses included different numbers of studies but showed overlapping findings in overall outcomes with our study.[3-5]

We also agree that one major limitation in our meta-analysis (and in other existing analysis on COVID-19) is the high heterogeneity of outcomes across studies. Therefore, when interpreting results of the total cohort of hematological malignancies, readers must take into account the relative overrepresentation of some conditions such as chronic lymphocytic leukemia and multiple myeloma, which may have been due to the prevalence as well as the need of rapid recruitment necessary for studies in this evolving pandemic, especially in the early phase. However, in the beginning, the general clinical question was how patients with hematological cancers react to vaccination, which may be particularly important for general patient counseling in the community setting. However, to account for certain confounders as much as possible, we aimed to dissect as many subgroups as possible to show possible differences in outcomes, which is a major limitation in other meta-analyses with fewer studies included. Another reason for heterogeneity may be introduced by the different testing platforms used. For this, we provided transparent information which platforms were used and reported in each study.

For the comparison between hematological and solid cancers, we specifically decided to report them as separate groups to minimize reporting bias when including only studies that used both groups as comparators. When only analyzing hematological and solid cancers / healthy controls in comparative fashion for overall response, the risk ratio was 0.76 (95% confidence interval [CI]: 0.69-0.84) and 0.70 (95% CI: 0.65-0.75) in favor of solid cancers and healthy controls, respectively. Regarding synthesizing other disease subgroups, we do not believe that this will be of utility for clinicians and community physicians, as such aggregated data also introduce selection bias. Therefore, we included hematological malignancies and then in a next step tried to report as many disease and treatment subgroups as possible. Of note, our analysis was done almost 1 year ago, new meta-analysis may aim to dissect outcomes in a more concise and detailed fashion.

Regarding suggested results for certain treatment platforms, myeloma patients receiving immunomodulatory drugs (IMIDs) showed an overall response of 81% (95% CI: 71-88). However, it should be highlighted that IMID-exposed patients may differ significantly, and reporting may be biased between studies, regarding regimens used that include IMIDs *versus* monotherapy or conditions in which treatment was applied (newly diagnosed *vs.* relapses *vs.* transplant / cellular therapy status). Results for proteasome inhibition could not be extracted reliably and was therefore decided not to be reported. Finally, follow-up period did not affect overall response outcomes.

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Disclosures

No conflicts of interest to disclose.

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