COMMENT & RESPONSE

SARS-CoV-2 Infections, Hospitalizations, and Mortality in Vaccinated Patients With Cancer in the US

To the Editor We have several concerns about the recent retrospective observational study in JAMA Oncology by Wang et al that demonstrated significant differences in COVID-19 breakthrough infection and subsequent hospitalization and mortality between fully vaccinated patients with or without cancer at baseline.

First, the possibility of collider bias should be considered in interpreting this result because the study focused on patients with full COVID-19 vaccination, and COVID-19 vaccination status might represent a collider associated with cancer and hospitalization. In this study, collider bias can develop when exposure (cancer status in this study) and outcome (COVID-19 and subsequent hospitalization in this study) each affect a third covariate, and the latter is unnecessarily controlled for in the analysis. To diminish this bias, it may be helpful to remove vaccine types from the propensity score matching process in sensitivity analysis.

Second, in addition to cancer, several other immune dysfunction conditions, such as solid organ transplantation, autoimmune disease, and HIV infection, carry a high risk of breakthrough SARS-CoV-2 infection. Also, those patients were encouraged to receive the SARS-CoV-2 vaccine. Therefore, we suggest that the authors exclude patients with other immunocompromised diseases to avoid confounding effects.

Third, to mitigate the effect of potential detection bias, the differences of loss of follow-up and the frequency of ambulatory visits could be included in the analysis either in the matching or adjustment process.

Finally, the treatment of COVID-19 could be different between patients with and without active cancer. Both antiviral agents (ritonavir-boosted nirmatrelvir and molnupiravir) and anti-SARS-CoV-2 monoclonal antibody are only recommended for nonhospitalized patients with mild to moderate COVID-19 who are at high risk of progressing to severe disease. In this study, patients with cancer were considered as the high-risk group and would receive these treatments. In contrast, patients without cancer may not receive them. Because these treatments would help prevent the progression of COVID-19, hospitalization, and mortality, their effect in this study should be clarified.

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