

# SARS-CoV-2 Vaccine Efficacy in Patients with Hematologic Malignancies: Practical Points for Further Research

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We thank Sriwijitalai and Wiwanitkit<sup>1</sup> for commenting on our article and giving us an opportunity to discuss our findings further.<sup>2</sup> The authors stated that although the immune responses to the SARS-CoV-2 vaccines could be impaired in patients with cancer, the possibility of asymptomatic COVID-19 before or after vaccination could interfere with the results. It should be noted that we specifically focused on seroconversion rates after vaccination in our paper.<sup>2</sup> However, the elements of the adaptive immune system, including B-cells, CD4+ T cells (especially T helper cells), and CD8+ T cells, play pivotal roles for the course, severity, and health outcomes in patients with COVID-19.<sup>3</sup> SARS-CoV-2-specific T-cell responses and rapid development of SARS-CoV-2 cross-reactive CD4+ T cells are critically important for the resolution of COVID-19 without major complications following primary infection by directing both the cellular and humoral immunity.<sup>4</sup> Therefore, further research should focus on measuring T-cell activity in addition to antibody responses to better define protection level against COVID-19 infection.

While we agree that the seronegative patients with cancer still have some level of protection and immunity against COVID-19,<sup>5</sup> we think that the development of an antibody response to vaccination is still very important in patients with cancer for several reasons. First of all, it was previously demonstrated that the neutralizing antibody response was highly predictive of immune protection against symptomatic COVID-19.<sup>6</sup> Additionally, Dispinseri et al. observed better survival with the development of an antibody response against SARS-CoV-2 earlier during the infection,<sup>7</sup> further supporting the surrogacy of antibody responses in COVID-19 protection. COVID-19 could create a mildly symptomatic and asymptomatic clinic in vaccinated patients. While the vaccination significantly reduced COVID-19 risk, two-thirds of the breakthrough infections were still symptomatic in a wide-scale study conducted on healthcare workers.<sup>8</sup> In contrast to the general population, the breakthrough COVID-19 infections could still lead to significant mortality and morbidity in patients with cancer,<sup>9,10</sup> pointing out a need for additional measures for COVID-19 prevention in patients with

cancer. Finally, other than increased COVID-19 mortality and morbidity, COVID-19 infection could lead to disruptions and delays in cancer care.<sup>11,12</sup> This issue could be particularly important for patients with hematological malignancies due to persistent viral shedding in these patients.<sup>13</sup> Therefore, even the protection of asymptomatic or mildly symptomatic COVID-19 infection is vital for patients with cancer, especially in patients under active treatment.

In conclusion, although the vaccination against COVID-19 is vital in patients with hematological malignancies, further research is needed for patients who did not develop seroconversion to prevent COVID-19 morbidity and mortality and COVID-19 related disruptions in cancer care.

## Conflict of Interest

Fatih M. Uckun: Ares Pharmaceuticals, LLC (employee). The other authors indicated no financial relationships.

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