Neutralizing Antibody Testing in Patients With Multiple Myeloma Following COVID-19 Vaccination

The International Myeloma Working Group recently held its annual summit (June 22-23, 2021), during which an in-depth discussion was conducted on COVID-19 vaccination and the response in patients with myeloma. The importance of this topic could not be overstated because patients with multiple myeloma (MM) are susceptible to infections as a result of intrinsic and therapy-related immunosuppression, older age, and presence of comorbidities. COVID-19 causes moderate to severe acute respiratory dysfunction in approximately 75% to 80% of patients with MM, resulting in death in almost one-third (range, 27%-57%) of hospitalized patients with myeloma and COVID-19 infection.1 Thus, vaccination against SARS-CoV-2 is the most important preventive strategy to protect patients with MM from COVID-19.

Data from recent studies suggest that a substantial proportion of patients with MM, especially those undergoing treatment with anti-CD38 or anti-B-cell maturation antigen (BCMA) therapies, do not develop anti-SARS-CoV-2 antibodies or have insufficient response even after full vaccination. Van Oekelen and colleagues2 reported that 16% of 260 patients with MM who were fully immunized with mRNA vaccines had undetectable IgG antibody titers against the spike-receptor binding domain of SARS-CoV-2 (using the US Food and Drug Administration [FDA]-approved COVID-SeroKlir Kantaro SARS-CoV-2 IgG test) at a median of 51 days after receiving the second mRNA vaccine dose. In contrast, all controls of similar age and gender had detectable anti-SARS-CoV-2 antibodies. The low antibody responses in patients with myeloma are not surprising because MM treatments directly target the very cells that generate the antibody responses. Of the 41 patients with no antibody responses, 24 (58.5%) were on anti-CD38 antibody–containing therapy at the time of posttreatment to help identify those patients at risk for severe COVID-19 and are likely to have suboptimal vaccine response, but we are not permitted to identify them. Therefore, we strongly recommend the use of NAb testing in all patients with myeloma under active treatment and in those who are receiving therapy with anti-CD38 or anti-BCMA–based regimens or within 6 months posttreatment to help identify those patients at risk for SARS-CoV-2 infection. This testing is probably best performed 4 weeks after completion of COVID-19 vaccination. We also recommend that similar studies be conducted for patients with other cancers who are receiving active chemotherapy to determine if reduced NAb responses similar to in MM are observed in specific subsets to identify groups that may benefit from testing for NAbs. We further recommend measurement of NAbs against SARS-CoV-2 as the best strategy. Although there is a good correlation between spike-receptor binding domain IgG antibodies and NAb titers (approximately 0.80) in the majority of the reported studies, NAb measurement is the best reflection of humoral immunity against the virus. Furthermore, recent data support that neutralization level against SARS-CoV-2 is highly predictive of immune protection; the neutralization level for 50% protection against detectable SARS-CoV-2 infection was 20.2% (95% CI, 14.4%-28.4%) of the mean convalescent level.5

Finally, what is the proper management for patients who lack a NAb response (vaccine failures)? We recognize that NAb production is just one part of the immune response to the vaccine. Although NAb titers correlate with protection to COVID-19, other elements of immune system (ie, T-cell responses) may be of importance for clinical protection against COVID-19. To date, and to our knowledge, we have no data for T-cell immunity after vaccination in patients with myeloma and its possible protection against COVID-19. Until these data are available, we recommend that patients who lack a NAb response should continue to
follow protective measures (eg, use of masks, social distancing) and be encouraged to participate in clinical trials (ie, with a third vaccine booster or protective administration of monoclonal antibodies against SARS-CoV-2).

While data are not available to determine whether patients with MM who received anti-CD38 or anti-BCMA strategies will mount an immune response with booster vaccinations, the Advisory Committee on Immunization Practices recently examined the data of 4 small studies of booster vaccine doses in immunocompromised individuals (eg, patients who have undergone solid organ transplant or who are undergoing dialysis). The results of these studies prompted the Advisory Committee on Immunization Practices and the CDC to recommend a booster shot of COVID-19 vaccines to be given to patients with chronic medical conditions, HIV infection, immunocompromised state, and cancer. While titer response has been shown to improve in patients with kidney transplantation, data are lacking in patients with MM. As a result, we cannot assume that a third dose will produce protective antibody levels against COVID-19 in patients with hematologic cancers who are undergoing active chemotherapy.

We agree that postvaccination COVID-19 titer testing is unnecessary for the general population, but it serves an important purpose for special patient populations, including patients with MM or other patients with severe immunosuppression (eg, chronic lymphocytic leukemia or lymphoma, especially for patients on anti-CD20-based regimens or taking Bruton kinase inhibitors). We urge the FDA and the CDC to review and adapt our recommendations for NAb titer testing in these special populations.

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REFERENCES