25% of Blood Cancer Patients May Not Respond to COVID-19 Vaccines

A study from the Leukemia & Lymphoma Society finds that antibody production varies widely across blood cancer types.

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A new study adds to the evidence that some people with blood cancers (hematologic malignancies) do not respond well to COVID-19 vaccines but finds that antibody production varies widely in this population, ranging from 100% for patients with smoldering multiple myeloma or hairy cell leukemia to just 44% for those with mantle cell lymphoma.

“Although some patients with hematologic malignancies will not mount a full antibody response compared to healthy individuals, vaccines are safe and offer protection to the majority of blood cancer patients,” Gwen Nichols, MD, chief medical officer of the Leukemia & Lymphoma Society (LLS), said in a press release. “But not everyone will be protected, and blood cancer patients are at increased risk of serious illness and death from COVID-19.”

People with weakened immunity, including certain cancer patients and organ transplant recipients who take immunosuppressive drugs, are at risk for more severe complications and death due to COVID-19. They can also have slower and weaker immune responses after natural infection or vaccination. Several recent studies have shown that most people with solid tumors have good antibody responses after receiving COVID-19 vaccines, but those with blood cancers, such as leukemia or lymphoma, don’t fare as well.

The new study (NCT04794387), by Nichols, LLS chief scientific officer Lee Greenberger, PhD, and colleagues, published in Cancer Cell, offers more detail, showing that response rates differ substantially among people with different hematologic malignancies.

This analysis looked at data from 1,445 blood cancer patients who had their antibodies against SARS-CoV-2 (the coronavirus that causes COVID-19) measured at least two weeks after the second dose of either the Pfizer-BioNTech or Moderna mRNA COVID-19 vaccine.

The study—the largest to date—was made possible by more than 8,000 current and former blood cancer patients who became “citizen scientists” and joined the LLS National Patient Registry, a collaboration between LLS and the consumer health care technology company Ciitizen, which provides an online medical records platform.

The researchers found that about 75% of blood cancer patients overall produced detectable antibodies after vaccination, while about 25% remained antibody-negative. According to LLS, this could leave nearly 250,000 blood cancer patients in the United States without inadequate protection.

Source: LLS National Patient RegistryLeukemia & Lymphoma Society

But, as shown in the illustration above, response rates varied dramatically among people with different hematologic malignancies.

People with multiple myeloma are as likely as the general population to have detectable SARS-CoV-2 antibodies: 95% of multiple myeloma patients overall, and 100% of those with smoldering multiple myeloma, responded.

Among people with lymphoma, those with Hodgkin lymphoma had a high likelihood of response (98%), but only 44% of those with mantle cell lymphoma had detectable antibodies. People with other types of non-Hodgkin lymphoma had response rates ranging from 62% to 85%.

Among people with leukemia, response rates ranged from 100% for those with hairy cell leukemia to 64% for those with chronic lymphocytic leukemia (CLL), the most common type in adults.

The vaccines were generally safe and well tolerated for people with blood cancer, who experience the same types of side effects—mainly injection site soreness and flu-like symptoms—as the

general population.

The type of cancer treatment patients receive appears to be key to vaccine response. People with certain types of leukemia and lymphoma are commonly treated with monoclonal antibodies—for example, Gazyva (obinutuzumab) or Rituxan (rituxumab)—that target the CD20 receptor on antibody-producing B cells. Others receive BTK inhibitors, such as Calquence (acalabrutinib) or Imbruvica (ibrutinib), which impair B-cell function. Some CAR-T immunotherapies target B cells directly, and the conditioning chemotherapy used prior to infusion of the genetically engineered T cells can wipe out all types of immune cells.

While vaccine response rates were lower among people who had recently undergone treatment, nearly 3 in 10 CLL patients who had not received any therapy during the past two years still did not produce antibodies, suggesting the disease itself may impair B-cell function. Six of the seven patients treated with B-cell-directed CAR-T therapy for CLL, diffuse large B-cell or follicular lymphoma were antibody-negative after vaccination, but four of five people who received a different type of CAR-T therapy for multiple myeloma had robust antibody responses.

Antibody responses do not give a full picture of immunity, however. Memory B cells (which produce antibodies against pathogens encountered in the past) and T cells also play a role. A recent study in Nature Medicine showed that T-cell responses contribute to protection even if antibody response is impaired. In this analysis, 77% of blood cancer patients with COVID-19 had detectable SARS-CoV-2-specific T-cell responses, and those with higher CD8 T-cell levels were more likely to survive, even if they were treated with B-cell-depleting therapy. All three COVID-19 vaccines authorized in the United States produce T-cell responses as well as antibody responses.

LLS experts say vaccination offers protection for a majority of blood cancer patients, but it should be combined with other prevention precautions.

“We encourage blood cancer patients to take every measure to protect themselves from COVID-19 by getting vaccinated and continuing to take preventative precautions,” Nichols said. “This includes wearing a mask, social distancing and avoiding crowds and poorly ventilated indoor spaces.” She advised patients who have been exposed to COVID to consult their doctor, as those who test positive for SARS-CoV-2 may be able to receive monoclonal antibodies that can keep them from getting sick. She also stressed that when others get vaccinated, they are not only protecting themselves but are also helping to protect people with weakened immune systems.

The Centers for Disease Control and Prevention is currently considering whether immunocompromised people, including cancer patients, could benefit from receiving an additional vaccine booster dose—an approach that has shown promise for organ transplant recipients.

“While we all want to go back to our pre-pandemic lives, that would be a big mistake for me,” said Larry Saltzman, a physician who leads the LLS National Patient Registry and is a longtime CLL survivor who has been treated extensively with B-cell-depleting therapies, including CAR-T. “I chose to get vaccinated as soon as the vaccine was available to me, and I continue to mask up

and take other precautions to make sure I’m here for my family, including my grandchildren.”

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