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Cancer Patients and Transplant Recipients Need Both COVID-19 Vaccine Doses

Natural immunity and vaccine responses may be weaker in people with immune suppression, so they should get their second dose promptly.

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A majority of people with cancer and organ transplant recipients are capable of mounting an immune response to the SARS-CoV-2 coronavirus and can gain immunity from COVID-19 vaccines, according to recent research. But people with immune suppression may have slower and weaker responses to natural infection or vaccination, so it is especially important that they get their second dose on schedule.

People with serious immune suppression are at risk for more severe complications and death due to COVID-19. This group includes cancer patients who use immune-suppressing therapy, transplant recipients who take immunosuppressive drugs to prevent organ rejection and people with AIDS (advanced, uncontrolled HIV disease).

It is well known that immunosuppressed people can have weaker immune responses to natural infection and vaccination, but SARS-CoV-2 immunity in this population is not well understood. What's more, cancer patients on treatment and other people with advanced immune suppression were generally excluded from COVID-19 vaccine trials (though people with well-controlled HIV could enroll).

Immune Response in Cancer Patients

Several studies over the past year have shown that people with cancer are, overall, more likely to develop severe COVID-19 and die from it. This is largely driven by people with lung cancer or blood cancers (such as leukemia and lymphoma), patients with advanced or metastatic cancer and people receiving immunosuppressive treatment.

Some blood cancers affect B cells—white blood cells that produce antibodies—and some types of treatment can lead to low white blood cell counts. In some reported cases, cancer patients with advanced immune suppression had prolonged SARS-CoV-2 infection, which provides an opportunity for viral variants to evolve.

As described in Nature Cancer, Astha Thakkar, MBBS, of the Montefiore Health System in New York City, and colleagues analyzed immune response to natural SARS-CoV-2 infection among people with cancer. In particular, they looked at the production of antibodies against the coronavirus spike protein, known as seroconversion.

This retrospective study included 261 cancer patients (average age 64 years) who were tested for two types of SARS-CoV-2 antibodies. Overall, they had a high rate of seroconversion—92% produced antibodies. However, significantly lower rates were seen for people with blood cancers (82%), stem cell transplant recipients (60%) and patients who received anti-CD20 monoclonal antibody therapies to treat leukemia or lymphoma (59%). In contrast, all 17 people who received checkpoint inhibitors or other immunotherapy had good antibody responses.

“We conducted the study out of our concern that cancer patients who develop COVID-19 may not benefit from the same degree of antibody protection as people without cancer, given that many are immunocompromised,” Thakkar said in a press release. “Our findings provide assurance that most people with cancer are able to mount an antibody response to the coronavirus that is similar to the general population. People with a history of cancer are likely as protected from reinfection as those without a history of disease and are likely to respond well to vaccines, according to our study.”

The National Comprehensive Cancer Network (NCCN) recommends that people receiving intensive chemotherapy for leukemia should delay vaccination until their white blood cell count recovers. Those undergoing stem cell transplants or CAR-T therapy should wait until three months after the procedure to improve the chances of having a good response. People undergoing major surgery should wait at least a few days. But everyone else should get vaccinated as soon as they can.

Don’t Delay Second Dose

A related study, however, raises concerns about vaccine response in people with cancer.

Leticia Monin-Aldama, PhD, of the Francis Crick Institute in London, and colleagues compared the safety and efficacy of one versus two doses of the Pfizer-BioNTech COVID-19 vaccine. In a Phase III clinical trial, this vaccine was 95% effective against symptomatic COVID-19 after the second dose, given three weeks after the first.

The Pfizer-BioNTech and Moderna mRNA vaccines provide substantial protection after the first dose, and the United Kingdom—in an effort to give more people partial protection as soon as possible—has adopted a strategy of delaying second doses for 12 weeks. This approach remains controversial, however, since a single-dose regimen was not tested in clinical trials. Health officials in the United States urge providers to stick with the authorized regimen of two doses given three or four weeks apart. (The Johnson & Johnson vaccine was tested and authorized as a single-dose regimen.)

This study, conducted in the United Kingdom, included 151 mostly elderly patients with solid tumors or blood cancers and 54 healthy control subjects who started the Pfizer-BioNTech regimen.

Most solid tumor patients had advanced disease; about 40% had received cancer treatment within the two weeks prior to their first vaccine dose, and just over half did so within the following two weeks.

Immune responses were compared between people who received a booster shot at three weeks versus those who did not. The researchers looked at antibody seroconversion and T-cell responses and analyzed antibody activity against both the original Wuhan SARS-CoV-2 strain and the B.1.1.7 variant.

As reported in a preprint that has not yet been peer reviewed, more than 90% of the healthy participants showed good immune responses after a single vaccine dose. But the proportion fell to 40% for people with solid tumors and to only 15% for those with blood cancers.

Looking specifically at antibody levels, the response rates were 97% for healthy people, 39% for solid tumor patients and 13% for blood cancer patients after the first dose. Efficacy among solid tumor patients "greatly and rapidly increased" by boosting with a second dose at three weeks. Doing so brought these patients up to a 95% response rate; however, if the booster was delayed by five weeks, there was little improvement. (There were too few blood cancer patients to draw clear conclusions.)

An analysis of T-cell responses in a subset of participants found that 82% of healthy people, 71% of solid tumor patients and 50% of blood cancer patients showed good T-cell activity after a single dose. T-cell immunity can potentially provide protection even if antibody responses are poor or diminish over time.

"Delayed boosting potentially leaves most solid and hematological cancer patients wholly or partially unprotected, with implications for their own health, their environment and the evolution of [variant] strains," the study authors concluded. "These data support prioritization of cancer patients for an early (21-day) second dose of the [Pfizer-BioNTech] vaccine."

Immune Response in Transplant Recipients

A third analysis, by Brian Boyarsky, MD, and colleagues from Johns Hopkins University School of Medicine, looked at COVID-19 vaccine responses among organ transplants recipients.

The study included 94 people who received kidney transplants, 51 who received liver transplants, 28 who received heart transplants, 18 who received lung transplants, two who had pancreas transplants and six who had other organ or multiple organ transplants. They were using a variety of immunosuppressive regimens to prevent rejection of the donor organ, mostly tacrolimus (83%), corticosteroids (54%) or mycophenolate (66%). Just over half received the Pfizer-BioNTech vaccine and the rest got the Moderna vaccine.

As described in JAMA, just 76 of the 436 participants (17%) had positive antibody responses at a median of 20 days after the vaccine first dose. People who received antimetabolite

immunosuppressive therapy were less likely to develop antibody responses, as were older patients. Interestingly, the response rate after the first dose was more than twice as high for those who got the Moderna vaccine compared with those who got the Pfizer-BioNTech vaccine.

“These findings of poor anti-spike antibody responses in organ transplant recipients after the first dose of mRNA vaccines suggest that such patients may remain at higher early risk for COVID-19 despite vaccination,” the study authors wrote. Going forward, the researchers said it will be important to analyze vaccines response, including memory B-cell and T-cell responses, after the second dose.

“From what we know, transplant patients cannot assume that they are safe after being vaccinated,” coauthor Dorry Segev, MD, PhD, told The Associated Press. “They may need postvaccination blood tests to be sure.”

Also speaking with the AP, David Mulligan, chief of transplant surgery and immunology at Yale University, said some people awaiting transplants might be able to hold off and get vaccinated first, while some who had transplants in the past could possibly cut back on their immunosuppressive temporarily. And—echoing the cancer researchers—he advised that immunocompromised transplant recipients should be sure to get both vaccine doses.

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