ABSTRACT

Patients with cancer and cancer survivors are vulnerable to infection, rendering vaccination a necessary intervention. The vaccination process represents a unique challenge in these populations—it is often impossible or impractical to delay the start of cancer treatment for immunizations, and vaccines may fail to trigger an appropriate protective immune response in immunocompromised patients and cancer survivors, with residual immune deficits. Additionally, live attenuated vaccines are contraindicated due to an increased risk of prolonged shedding and disease presence. The current NCCN Guidelines for Survivorship, which reflect the most up-to-date, evidence-based data relating to survivorship, detail the appropriate immunization practices in these highly susceptible populations.

While under active treatment, patients with cancer are vulnerable to infection, as chemotherapy, radiation therapy, and immune-altering therapies can lead to neutropenia, lymphopenia, and altered immune competence,” commented Maria Alma Rodriguez, MD, Professor of Medicine, and Director, Cancer Survivorship Programs, The University of Texas MD Anderson Cancer Center. “Immune deficits can persist for months or even years after treatment.” This seems to be particularly true in cancer survivors who underwent organ or hematopoietic stem cell transplantation, CAR cellular therapies, monoclonal antibody treatment, or long-term immune maintenance therapies, as well as in those without recovery of normal bone marrow function after undergoing chemotherapy. At the NCCN 2022 Annual Conference, Dr. Rodriguez emphasized the importance of appropriate vaccination practices in these highly susceptible populations.

General Principles of Immunization

“The first key principle of the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Survivorship: Immunizations and Infections is that we should review with our patients their immunization history and recommend that they update and receive any vaccines that they are missing and that are appropriate for their age and health conditions,” Dr. Rodriguez remarked. “In addition, these vaccines should preferably not be live.” In all cancer and transplant survivors, clinicians should encourage the administration of vaccines formulated from inactivated microorganisms, purified antigens, or other bacterial components; genetically engineered recombinant vaccines are also recommended in these high-risk populations.¹

Second, if possible, all indicated vaccines should be administered before the initiation of cancer treatment. Per the NCCN Guidelines, inactivated or recombinant vaccines should be given at least 2 weeks before. A consultation with an infectious disease specialist is recommended before administering live vaccines; if this type of immunization is deemed necessary, it should occur at least 4 weeks before any treatment is initiated.¹

Both the live and inactivated or recombinant vaccines may be given at least 3 months after the completion of chemotherapy. In cancer survivors who underwent hematopoietic blood stem cell transplantation, cellular therapy, or anti–B-cell antibody therapy, the guidelines recommend delaying the administration of both types of vaccinations for at least 6 months after chemotherapy and the last dose of such therapy.¹

Challenges to Vaccination

In cancer and transplant survivors, the vaccination process represents a unique challenge. It is often impossible or impractical to delay the start of treatment; thus, according to Dr. Rodriguez, there may not be adequate time to allow for immunizations. Furthermore, vaccinations may not trigger an appropriate protective immune response in immunocompromised patients and cancer survivors, with residual immune deficits.¹

Certain vaccines, such as those that are live attenuated, are contraindicated in immunosuppressed patients and in those who are in close contact with the patient due to an increased risk of prolonged shedding and disease presence. Per the NCCN Guidelines, when other vaccine options exist, they should be preferred in cancer survivors.¹
Risk Assessment and Interventions

“In addition to the anticipated risk due to the cancer treatments—that is, namely, chemotherapy, radiation therapy, cellular therapies, or monoclonal antibodies that can alter immunity—there are numerous other clinical and social factors that should be considered in the patient’s history,” Dr. Rodriguez commented. Comorbidities, such as chronic lung disease, diabetes, cardiomyopathies, and chronic renal conditions, are associated with a higher risk of developing an infection. Patients who underwent splenectomy or require transfusions, in addition to those who were recently exposed or anticipate exposure to infectious disease, may also have increased vulnerability. Certain occupational fields carry an increased risk for infection as a consequence of interactions. Cytotoxic chemotherapy, monoclonal antibodies, radiation therapy, corticosteroid treatment, prior cellular therapies, and CAR T-cell therapy are also classified as risk factors for infection in the NCCN Guidelines.¹

“There are a number of social factors that are also important and relevant to ask, as they carry unique risks,” Dr. Rodriguez commented. “[This includes] certain sexual behaviors, illicit drug use, and housing conditions.”

Interventions that may decrease the risk of infection include vaccination, education on prevention practices, and antimicrobial prophylaxis. The NCCN Guidelines recommend assessing overall immune system viability and history of allergic reactions before vaccination (Figure 1).¹

According to Dr. Rodriguez, the NCCN Guidelines summarize the key vaccination recommendations for all cancer survivors and those with special circumstances or risk factors (Figure 2). She noted that cancer survivors who anticipate travel should consult with a specialist, as the NCCN Guidelines do not provide these particular vaccination recommendations.¹

Current Topic of Interest: Vaccination Against Respiratory Infection

Before the COVID-19 pandemic, the influenza virus was a leading concern due to its role in the development of pneumonia. However, in 2020, COVID-19 ranked as the third most common cause of death in the US population. Other respiratory infections, namely influenza and pneumonia, ranked 9th among the top 10 causes of death.² “Respiratory infections, sadly, have a high-ranking place in the top 10 causes of mortality in the United States,” Dr. Rodriguez remarked. “When combined, the number of deaths from COVID and other respiratory infections is nearly as high as that of cancer.”²,₃ Older patients and those residing in rural locations have been found to experience high rates of respiratory infection–related mortality.³,₅

In the United States, both the live and recombinant influenza virus vaccines are recommended to prevent pneumonia. The nasally administered live formulation is contraindicated in pregnant women, patients aged ≥50 years, and those with compromised immunity. Metastatic malignancies, Hodgkin and non-Hodgkin lymphomas, multiple myeloma, leukemia, and cancer therapy–induced iatrogenic immunosuppression are among the conditions considered by the CDC as immune-compromising. According to Dr. Rodriguez, injectable recombinant formulation of the influenza vaccine is indicated for all ages and is recommended in patients with cancer and cancer survivors; their caregivers and household members should also be immunized for optimal protection.¹

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**Figure 1.** NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Survivorship: risk assessment and screening and interventions [SIMIN-2]. Version 1.2022. ©2022 National Comprehensive Cancer Network, Inc. All rights reserved. These guidelines and this illustration may not be reproduced in any form without the express written permission of NCCN®. To view the most recent and complete version of these NCCN Guidelines, go to NCCN.org.
Infection with pneumococcal bacteria is another common cause of pneumonia, Dr. Rodriguez noted. In addition to the existing 23-valent pneumococcal polysaccharide vaccine, the newly approved 15- and 20-valent pneumococcal conjugate vaccines are indicated in adults. Only one formulation, the 13-valent pneumococcal conjugate vaccine, may be administered to children.6

“The algorithms for timing and combination of prior and newer vaccines are complicated, particularly for those who have been previously vaccinated,” Dr. Rodriguez said. For those who are unvaccinated, “the key issue is the distinction between those [with and without] clinical conditions.” In the absence of clinical conditions, vaccination against pneumococcal pneumonia is indicated only in patients who are aged ≥65 years. According to Dr. Rodriguez, in those with underlying clinical conditions, the vaccination algorithm may be applied between the ages of 19 and 64 years and repeated at ≥65 years.6

Vaccination against the current leading cause of pneumonia, COVID-19, is recommended by NCCN and the CDC in patients with cancer and cancer survivors.1,7 The available mRNA vaccines are currently preferred for adults who are moderately or severely immunocompromised.7 However, as new data become available, the “NCCN: Cancer and COVID-19 Vaccination” document8 and CDC website should be consulted for updated guidance.

**Other Updated Vaccine Indications**

The inactivated tetanus, diphtheria, and acellular pertussis (Tdap) vaccine is usually administered during childhood. However, per the NCCN Guidelines, it may be administered in adults of any age and is considered safe for all cancer and transplant survivors and close contacts, with boosters every 10 years.1

The recombinant shingles vaccine, which is currently the only available formulation in the United States, was found to be safe and effective in cancer survivors and their close contacts who are aged ≥50 years. Of note, the NCCN Guidelines were recently updated to recommend this vaccine in patients between the ages of 19 and 49 years who are or will be immune-deficient or immunosuppressed because of disease or therapy.1 “Therefore, this is a vaccine to consider for patients prior to the treatment initiation,” Dr. Rodriguez explained.

The inactivated hepatitis A and recombinant hepatitis B vaccines are indicated for patients with certain clinical and social conditions that may increase their risk of contracting the viruses; these formulations are also considered to be safe for cancer survivors and close contacts. Recently, the indication of the hepatitis B vaccine was expanded to include all adults between ages 19 and 59 years. According to Dr. Rodriguez, it may also be considered for patients with medical or social risk factors who are aged ≥60 years.1

The NCCN Guidelines recommend the cancer-preventing recombinant HPV vaccine in patients aged 9–26 years. However, based on shared decision-making, the indication was extended to those aged 27–45 years. Furthermore, the HPV vaccine is deemed safe for cancer survivors and their close contacts.1

The *Haemophilus influenzae* type b and meningococcal vaccines have unique applications in patients with...
asplenia, as well as in stem cell transplant recipients, according to Dr. Rodriguez. After transplantation, the inactivated polio vaccine should also be administered.1

Live attenuated vaccines—such as measles, mumps, and rubella (MMR), oral typhoid, yellow fever, rotavirus, nasal influenza, and varicella—are contraindicated or should be used with caution in actively immunocompromised cancer survivors and their close contacts. Per the NCCN Guidelines, live attenuated vaccines may be offered to these populations only on clearance from a clinician experienced in immunization procedures or an infectious disease specialist.1

“The [NCCN Guidelines have] a comprehensive table that lists the vaccines, the patient populations for whom they are recommended… and the timing of the vaccines as well as the dose schedules,” Dr. Rodriguez commented. An additional table outlines the vaccines considered safe for cancer and transplant survivors and close contacts. “[These tables are] designed to consolidate… all of the relevant information, and [are] intended to be a reference for your practice.” These tables can viewed online, in these guidelines, at NCCN.org [SIMIN-B, 1 and 2 of 5].

Disclosures: Dr. Rodriguez has disclosed having no relevant financial relationships.

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References