**Recommendations of the NCCN COVID-19 Vaccination Advisory Committee***

- Patients with active cancer and those on treatment should be prioritized for vaccination and should be immunized when any vaccine that has been authorized for use by the FDA is available to them.
- Immunization is recommended for all patients receiving active therapy, with the understanding that there are limited safety and efficacy data in these patients.
- Reasons for delay of vaccines are similar to those that impede delivery to the general public (eg, recent exposure to COVID-19), and there are also cancer-specific factors. Vaccination should be delayed for at least 3 months following hematopoietic cell transplantation (HCT) or engineered cellular therapy (eg, chimeric antigen receptor [CAR] T-cells) to maximize vaccine efficacy.
- Caregivers and household/close contacts should be immunized whenever possible.
- The committee supports use of any of the available EUA approved vaccines (Pfizer/BioNTech [BNT162b2 mRNA vaccine], Moderna [mRNA-1273 SARS-CoV-2 Vaccine] and Janssen/Johnson & Johnson [Ad26.COV2.S Adenovirus vector vaccine]) in patients who are eligible.

### Table 1. COVID-19 Vaccination Recommendations for Cancer Patients

<table>
<thead>
<tr>
<th>Patients Treatment/Cancer Type</th>
<th>Timing**†,¶</th>
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</thead>
<tbody>
<tr>
<td><strong>Hematopoietic Cell Transplantation (HCT)/Cellular Therapy</strong></td>
<td></td>
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<tr>
<td>Allogeneic transplantation</td>
<td></td>
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<tr>
<td>Autologous transplantation</td>
<td></td>
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<tr>
<td>Cellular therapy (eg, CAR T-cell)</td>
<td>At least 3 months post-HCT/cellular therapy**†,¶</td>
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<tr>
<td><strong>Hematologic Malignancies</strong></td>
<td></td>
</tr>
<tr>
<td>Receiving intensive cytotoxic chemotherapy (eg, cytarabine/anthracycline-based induction regimens for acute myeloid leukemia)</td>
<td>Delay until absolute neutrophil count (ANC) recovery**¶</td>
</tr>
<tr>
<td>Marrow failure from disease and/or therapy expected to have limited or no recovery</td>
<td>When vaccine available</td>
</tr>
<tr>
<td>Long-term maintenance therapy (eg, targeted agents for chronic lymphocytic leukemia or myeloproliferative neoplasms)</td>
<td>When vaccine available**¶</td>
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<tr>
<td><strong>Solid Tumor Malignancies</strong></td>
<td></td>
</tr>
<tr>
<td>Receiving cytotoxic chemotherapy</td>
<td>When vaccine available**¶</td>
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<tr>
<td>Targeted therapy</td>
<td>When vaccine available</td>
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<tr>
<td>Checkpoint inhibitors and other immunotherapy</td>
<td>When vaccine available**¶</td>
</tr>
<tr>
<td>Radiation</td>
<td>When vaccine available</td>
</tr>
<tr>
<td>Major surgery</td>
<td>Separate date of surgery from vaccination by at least a few days**¶</td>
</tr>
<tr>
<td><strong>Caregivers and Household/Close Contacts (≥16 years of age)</strong></td>
<td>Any time eligible to receive the vaccine**¶</td>
</tr>
</tbody>
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**†** COVID-19 vaccines should be prioritized over other needed vaccines, as data on dual vaccination are not available to date. Fourteen days are recommended between COVID-19 vaccines and other approved vaccines. 

**‡** Discussion with clinical trial leads should be considered in advance to prevent protocol violations or exclusions. 

**¶** CDC recommendations for timing of vaccination post-COVID-19 infection (after removal from isolation [minimum ≥20 days for cancer patients]), and/or post-SARS-CoV-2-specific monoclonal antibody or SARS-CoV-2 convalescent plasma (after 90-days).
PRIORITIZATION AMONG CANCER PATIENTS IN THE SETTING OF LIMITED VACCINE AVAILABILITY:

If there are limits to supply, prioritization may need to be considered for cancer patients. Prioritization is challenging to develop when considering the diverse population of patients with their varied comorbidities, demographic and social factors known to increase risk of COVID-19 acquisition, morbidity, and/or mortality. Decisions must be made in accordance with state and local vaccine guidance on allocation. The following criteria can be used to help determine local guidance to consider when developing such decisions*:

1) Prioritize patients with active cancer on treatment (including hematopoietic and cellular therapy), those planned to start treatment, and those immediately (<6 months) post-treatment, except those receiving only hormonal therapy.

2) Consider additional risk factors for such patients and other factors linked to adverse COVID-19 complications including, but not limited to:
   a. Patients with advanced age (eg, ≥65 years of age)
   b. Patients with comorbidities (eg, chronic pulmonary, cardiovascular, or renal disease)
   c. Social and demographic factors that include poverty, limited access to health care, and underrepresented minorities

*The current vaccine recommendations and prioritization guidelines will be updated regularly based on availability of new data. There are important gaps in knowledge on vaccine immunogenicity in specific patients with cancer and therapies. We may learn that specific therapies limit vaccine efficacy and would warrant vaccine delay. The durability of vaccine protection is being investigated in the general population and is expected to be attenuated in immunocompromised patients with cancer.

Table Footnotes

a) Graft-versus-host disease (GVHD) and immunosuppressive regimens to treat GVHD (eg, systemic corticosteroids and targeted agents) are expected to blunt immune responses to vaccination. Delay of vaccination until immunosuppressive therapy is reduced and/or based on immunophenotyping of T-cell and B-cell immunity can be considered.

b) Patients on maintenance therapies (eg, rituximab, Bruton tyrosine kinase inhibitors, Janus kinase inhibitors) may have attenuated response to vaccination (see below).

c) The committee recognizes that granulocytopenia does not, in itself, significantly affect immunologic response to vaccination. It is used in this setting of profound immunosuppression for patients with hematologic malignancies as a surrogate marker for recovery of adequate immunocompetence to respond to vaccines and sufficient platelet recovery to avoid bleeding complications from intramuscular administration. Due to short periods of neutropenia among solid tumor malignancies this is not used for timing of vaccination.

d) In patients receiving chemotherapy, optimal timing of vaccination in relation to cycles of chemotherapy is unknown. Given the variability of specific regimens and intervals between cycles, it is not possible to state whether immunization will be more effective if administered at the time of chemotherapy administration versus mid-cycle when the white blood cell (WBC) count might be at its nadir. In the absence of data, we recommend vaccination when available.

e) Theoretical risk of exacerbated immune-related adverse events in patients receiving immune checkpoint inhibitors; there are no data on timing of vaccine administration, so this may be considered on the same day as immunotherapy for convenience and to reduce added visits to the office whenever possible.

f) The primary reason for avoiding vaccine in the perioperative period is so that symptoms (eg, fever) can be correctly attributed to surgery versus vaccination. For more complex surgeries (eg, splenectomy or which may lead to an immunosuppressive state) surgeons may recommend a wider window (+/- 2 weeks) from the time of surgery.

g) Even if vaccinated, close contacts should continue to wear masks, maintain social distancing guidelines, and follow other recommendations for COVID-19 prevention.
OVERVIEW:
Large cohort studies have demonstrated that cancer patients are at high risk for COVID-19–associated complications. As an at-risk population, there is a clear need for vaccinating these patients to avoid excess morbidity and mortality during the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic. In addition, since immunosuppressed patients may be sources of prolonged viral shedding and development of variants, prioritizing vaccinations to these vulnerable patients may provide an additional societal benefit. Individuals with active cancer or with active, recent (<6 months), or planned cancer treatment should be considered highest priority to receive one of the currently available COVID-19 vaccines that have been approved by FDA emergency use authorization (EUA).

The National Comprehensive Cancer Network (NCCN) COVID-19 Vaccination Advisory Committee feels strongly that COVID-19 vaccines should be given to all cancer patients, as well as household contacts and caregivers, when they are eligible to receive the vaccine; the committee has no preference for any of the approved vaccines. Recognizing the limited clinical data available in cancer patients, individuals should be vaccinated with the highest priority group for which they qualify. Finally, data from vaccine trials have demonstrated that vaccines decrease the incidence of COVID-19 disease and complications, but there are limited data that suggest that these vaccines may prevent SARS-CoV-2 infection and subsequent risk of transmission. Therefore, even if vaccinated, patients and close contacts should continue to wear masks, maintain social distancing guidelines, and follow other recommendations for COVID-19 prevention.

Due to limitations in prospective data relating to vaccination use in patients with active malignancy, recommendations are based on the expert opinion of the committee; as data emerge our approach will be modified accordingly. Decisions about when to offer COVID-19 vaccines should be based on local availability, while taking into account the National Academies of Sciences, Engineering, and Medicine (NASEM) Framework for Equitable Allocation of COVID-19 Vaccine that includes: risk of infection, severe morbidity and mortality, excess burden of COVID-19 on specific communities, and transmission to others. The key principles are as follows:

1. There are limited data for these vaccines in patients with cancer. There is a priority to generate data for this population, especially in those receiving active cancer therapy.

2. Persons with active cancer are at increased risk of complications from SARS-CoV-2, and efforts to limit spread in high-risk patients at cancer centers is imperative. Cancer centers should be specified locations where vaccine should be allocated to allow safe delivery to these high-risk patients.

3. A simple and rapid approach to vaccination is important.

4. Vaccine should be offered to cancer patients in a manner to assure inclusion of racial/ethnic minorities, non-English–speaking patients, and other at-risk groups (eg, patients with disabilities) to ensure equity in COVID-19 vaccine distribution; health care systems should make special efforts to take into consideration social vulnerability markers that have been demonstrated during this pandemic.

5. There are no reports of increased risk for side effects of the COVID-19 vaccines in patients with cancer as compared to the general population, but published safety data are not currently available for cancer patients. Despite this gap in knowledge, we strongly recommend that patients with cancer receive vaccination when offered given their increased risk of morbidity and mortality from COVID-19.
6. Vaccine efficacy in the setting of cancer care and a weakened immune system is unknown.

7. Those immediately around patients under cancer care (eg, spouses, household members) are the most likely to be sources of transmission and should be considered for early vaccination.

**Vaccine Safety and Efficacy in Cancer Patients:**
Cancer patients should be counseled that although these vaccines have been shown to be safe and effective in the general population, data on their effectiveness in immunosuppressed patients is unknown. Current SARS-CoV-2 mRNA vaccines (e.g. Pfizer/BioNTech, Moderna) do not contain live virus and do not pose an immediate safety risk for immunosuppressed patients. The available single dose SARS-CoV-2 viral vector (Adenovirus 23 [Adv]) vaccine (Janssen/Johnson & Johnson) is safe for use in immunosuppressed hosts, as the adenovirus vector has been modified to make it replication incompetent. It is important, however, that providers know that immunosuppressed patients will likely have blunted immune responses when compared to the general population and thus should receive education regarding the importance of following all current prevention guidance post-vaccination. Caregivers and household/close contacts should be strongly encouraged to get vaccinated when the vaccine is available.

All three vaccines have been shown to be safe in the general population, although post-vaccination arm soreness, fatigue, fever and headache, among other side effects are not uncommon; data regarding post-vaccination side effects in cancer patients have not been described to date. Anaphylaxis has been reported with both mRNA vaccines, although incidence is very low, ranging from 2.5-4.9 cases per million doses administered.

**Post-vaccine lymphadenopathy and Imaging Studies in Cancer Patients:** Reactive lymphadenopathy has been reported in up to 16% of the patients following COVID-19 vaccination with the mRNA (Pfizer/BioNTech, Moderna) vaccines; this side effect has not been reported to date with the Adv vector vaccine (Janssen/Johnson & Johnson). To reduce the number of unwarranted biopsies, several reports with guidance on imaging studies have been published. Vaccination history and site of injection should be included in medical history to provide the radiologists with the clinical background for accurate interpretation. The Society of Breast Imaging recommends consideration of scheduling screening breast imaging 4-6 weeks following the completion of the COVID-19 vaccination, when possible. Unilateral lymphadenopathy noted on chest CT may likely be reactive following the vaccine unless it persists beyond six weeks following the second dose of the vaccine; abnormal FDG update with PET scanning has also been reported. With the currently available data, we recommend delay of imaging studies by 4-6 weeks following the COVID-19 vaccine if it will not result in a delay that will affect patient outcomes. For patients whose scans cannot be delayed in relation to the vaccination, careful consideration of the clinical context should be made by the treating oncologists and radiologists when interpreting the imaging studies. For patients who have a history of breast cancer, the vaccine should be administered in the contralateral arm whenever possible.

**Antibody Testing Post-Vaccination:**
Emergency use authorized (EUA) vaccines have not been systematically evaluated in patients with active cancer or recipients of cellular therapy (hematopoietic cell transplant/ chimeric antigen receptor T-cell) as these populations were mostly excluded from clinical trials; although both the Pfizer/BioNTech and Janssen/Johnson & Johnson vaccine clinical trials did include cancer patients. Assessment for long-term immunity after vaccination with serologic testing (against spike protein of SARS-CoV2) in the cancer
The correlation between antibody titers (against spike protein) and immunity as well as longevity of protection is not known at this time. Additionally, it is postulated that vaccine induced T-cell immunity may play a role in protection. Immunologic data from trials are still pending and at present standardized commercially available assays evaluating T-cell responses are lacking. Furthermore, the diversity of antibody tests, include non-vaccine targets such as the viral nucleocapsid, make interpretation of results even more complicated. The committee does not recommend routine post-vaccine antibody testing. Antibody testing and evaluations of post-vaccine T-cell responses should only be done under research protocols.

PRIORITIZATION AMONG CANCER PATIENTS IN THE SETTING OF LIMITED VACCINE AVAILABILITY:
COVID-19 vaccine availability varies in different regions, state mandates change frequently, and limitations exist for ability to vaccinate large populations efficiently. These realities may necessitate prioritization of an order in which patients with cancer are offered immunization. This prioritization must be evidence-based but also values-based as possible; even so, debate and disagreements exist. In situations of vaccine shortage, risk factors for COVID-19–related morbidity and mortality (eg, advanced age, chronic lung disease, cardiovascular disease) and cancer-specific factors should be considered in prioritization. Those with active cancer and/or therapy should be prioritized over those who completed therapy and those without evidence of disease. We acknowledge that this point is subject to debate, as one could argue that COVID-19 immunization would be most effective and impactful in patients with a history of cancer who are now without evidence of disease as compared to patients with advanced cancer with limited life expectancy and unknown immune responses to vaccination. Among NCCN Panel members, some centers use scoring systems to prioritize patients for vaccination that include age, comorbidities, metastatic disease, and hematologic versus solid tumor malignancies. Despite the generally worse prognosis of COVID-19 in patients with hematologic malignancies that would justify prioritizing these patients for vaccination, a competing concern is that these patients may mount a less effective immune response to vaccination. In the absence of data on vaccine immunogenicity, the panel cannot currently recommend prioritization of patients based on hematologic versus solid tumors. Similarly, the panel cannot issue a recommendation on prioritization based on chemotherapy, surgery, radiation, targeted therapy, or immunotherapy; however, patients without active cancer who are receiving hormonal therapy only would have lower prioritization.

National advocacy to allow administration of COVID-19 vaccines to patients participating in ongoing clinical trials is needed. Patients currently being treated on clinical trials, or considering enrollment on a clinical trial should not defer COVID-19 vaccination, or be ineligible for enrollment or continuation on a clinical trial because of COVID vaccination, unless there is a specific scientific contraindication. The same should apply to COVID-19 antibody treatment. Clinical trials currently ongoing or nearing initiation should allow for COVID-19-related interventions without excluding candidacy or ongoing participation.

SOCIETAL CONSIDERATIONS:
As vaccine allocation and prioritization efforts are underway, it is imperative that patients have equitable access to the vaccines. The NASEM guidelines have recommended the incorporation of social vulnerability indices to mitigate health inequities that have clearly arisen during the COVID-19 pandemic. Notably, similar to the general non-cancer population, Black/African American, Hispanic/Latino, and Native American patients with cancer have been observed to have increased risk of
developing COVID-19. Consequently, we encourage health systems to incorporate social vulnerability markers tailored to their populations to address the myriad of health inequities that have arisen during this pandemic. In addition, patients who may not have access to electronic health record platforms or email should be considered when vaccine invitation and scheduling are being operationalized. Special efforts should also be made to engage and incorporate those patients with limited English proficiency. Finally, health systems are encouraged to collect—to the extent possible—both race-ethnic and socioeconomic data for patients who receive the vaccine, so that these data can be periodically reviewed, and if inequities develop, aggressively addressed.

**POST-VACCINE PREVENTION:**
Despite recent recommendations from the CDC for loosening some restrictions for the general public ≥ 2 weeks after completion of COVID-19 vaccination (2 weeks post second dose for Pfizer/BioNTech and Moderna, 2 weeks after first dose of Janssen/Johnson & Johnson), the committee recommends continued vigilance as data on efficacy of these vaccines in cancer patients remains unknown. As cancer patients may remain at increased risk for COVID-19 complications and may have less protection from vaccines, patients and close contacts should continue to wear masks, maintain social distancing, avoid crowds and follow guidelines and other recommendations for COVID-19 prevention even after vaccination. Future studies on boosters/re-vaccination are expected.

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