Recommendations for COVID-19 Vaccination in Patients with Cancer

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Objectives

1) **Discuss the recommendations of the National Comprehensive Cancer Network (NCCN) Advisory Committee on COVID-19 Vaccinations**
2) **Review the safety and efficacy of the COVID-19 vaccines in patients with cancer**
3) **Recognize other special considerations in vaccinating against COVID-19 in patients with cancer**

Background

- Patients with cancer are at high risk for COVID-19-associated complications
- Higher risk morbidity and mortality
- Limiting disease in immunosuppressed patients with cancer provides societal benefit
  - Sources of prolonged viral shedding
  - Development of variants
- NCCN Committee recommends that COVID-19 vaccines should be given to all patients with cancer, as well as household contacts and caregivers, when they are eligible to receive the vaccine
- COVID-19 vaccine is inactive → safety < efficacy balanced with need of vaccine
- NCCN provides guidance on proper timing and specific considerations for patients with cancer

NCCN: Cancer and COVID-19 Vaccination. Version 5.0, January 4, 2022.

EUA and/or FDA Approved COVID-19 Vaccines

Manufacturer	Technology	Interval between doses	Approval	Third dose	Booster
Pfizer (BNT162b2)	mRNA	21 days	• FDA approved ≥16 years • Under EUA for persons aged 5–15 years • Children <12 years =pediatric formulation	At ≥ 4 weeks after primary series	5 months
Moderna (mRNA-1273)	mRNA	28 days	FDA approved for those ≥18 years	At ≥ 4 weeks after primary series	5 months
Jansen/J&J (Ad26.COV2.S)	Vector vaccine (human adenovirus 26)	Single Dose	Under EUA for those ≥18 years	2 months, 2 doses 28 days apart	6 months

J&J = Johnson & Johnson
Food and Drug Administration (FDA). May 25, 2021. Accessed February 7, 2022. https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines.
NCCN: Cancer and COVID-19 Vaccination. Version 5.0, January 4, 2022.

NCCN Vaccination Recommendations in Patients with Cancer

NCCN Recommendations

- Reiterates the need for patients with cancer to be fully immunized, including receiving third doses and boosters
- Vaccination is also recommended for caregivers, household/close contacts, and the general public.
- Supports use of any of the available FDA-approved or EUA vaccines
  - CDC-ACIP
    - Prefers mRNA vaccines over the J&J vaccine
    - NCCN supports recommendations
- Strongly supports mandates for health care worker vaccination

CDC = Centers for Disease Control; ACIP = Advisory Committee on Immunization Practices; J&J = Johnson & Johnson
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NCCN: Timing Vaccines WRT Treatment/Cancer Type

Patients Treatment/Cancer Type	Timing to Start Series
Hematopoietic Cell Transplantation (HCT)/Cellular Therapy	
Allogeneic transplantation	At least 3 months post HCT/cellular therapy
Autologous transplantation	
Cellular therapy (eg, CAR T cell)	
Hematologic Malignancies	
Receiving intensive cytotoxic chemotherapy (eg, cytarabine/anthracycline-based induction regimens for acute myeloid leukemia)	Delay until absolute neutrophil count (ANC) recovery or for those not expected to recover, as soon as possible
Marrow failure from disease and/or therapy expected to have limited or no recovery	As soon as possible
Long-term maintenance therapy (eg, targeted agents for chronic lymphocytic leukemia, myeloma, or myeloproliferative neoplasms)	As soon as possible
Solid Tumor Malignancies	
Receiving cytotoxic chemotherapy	As soon as possible
Targeted therapy	
Checkpoint inhibitors and other immunotherapy	
Radiation	
Major surgery	Separate date of surgery from vaccination by at least a few days
Caregivers and Household/Close Contacts → Any time eligible to receive the vaccine	

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Few Additional Vaccine Timing Considerations

- CDC recommendations
  - Post-SARS-CoV-2–specific monoclonal antibody or SARS-CoV-2 convalescent plasma → after 90 days
  - Post-COVID-19 infection (after removal from isolation) → minimum ≥20 days for patients with cancer

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NCCN: Additional Dose Recommendations for Immunocompromised Patients

- Fully supports a third dose for immunocompromised patients ≥ 12 years of age
  - Preference to utilize the mRNA vaccines
  - Initial J&J adenovirus vector vaccine–based COVID-19 vaccine → a second dose of the J&J vaccine or an mRNA vaccine **(preferred)**
- Dosing of Additional Dose?
  - Full dose for both mRNA vaccines

J&J = Johnson & Johnson
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NCCN: Timing of this Additional Dose

- After mRNA 2-dose series complete → ≥ 4 weeks administer same or available mRNA vaccine
- After J&J vaccine → 2 months with mRNA vaccine preferred over a J&J vaccine
- For those who received one J&J dose
  - National Guidance → single additional dose
  - NCCN Committee
    - Two additional doses
      - For high-risk patients
      - At least 28 days apart
    - Booster at least 6 months after third dose

J&J = Johnson & Johnson
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NCCN: Third Dose Vaccine for Immunocompromised Versus Booster Vaccines for the General Public

- Third dose = full dose
- Boost dose
  - Half dose for Moderna
  - Full dose for Pfizer
- mRNA boosters are to be administered 5 months* after initial dose series

* 5 months is a CDC update from 6 months

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NCCN: Specific Criteria for additional dose of mRNA vaccines for moderately to severely immunocompromised people

- Recognizes CDC recommendations including:
  - Those who have been receiving active cancer treatment for tumors or cancers of the blood
  - Those who have received an organ transplant and are taking medicine to suppress the immune system
  - Those who have received an HCT within the last 2 years or are taking medicine to suppress the immune system
  - Those with moderate or severe primary immunodeficiency (such as DiGeorge syndrome or Wiskott-Aldrich syndrome)
  - Those with advanced or untreated HIV infection
  - Those on active treatment with high-dose corticosteroids or other drugs that may suppress immune response

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NCCN recommendations: How to prioritize additional dose for patients with cancer

- Solid tumor malignancies
  - Those receiving therapy, now or future, within a year of vaccine administration
    - Applies to all cancer therapies
    - Excludes non-melanoma skin cancers or superficial lesions treated solely with local therapy
- All hematologic malignancies regardless of active therapy
  - Poor serologic responses
    - Immunodeficiency due to the malignancy itself
    - Immunodeficiency due to cancer therapy
- Hematopoietic cell transplant and cellular therapy
  - Prioritize those who are ≤2 years post-procedure
  - All allogeneic HCT recipients actively on immunosuppressive therapy or with any history of GVHD regardless of time post-transplant
- Cancer with other immunosuppressive conditions not meeting criteria
  - Examples: HIV infection or autoimmune disorders
  - Immunosuppressive therapy separate from cancer therapy

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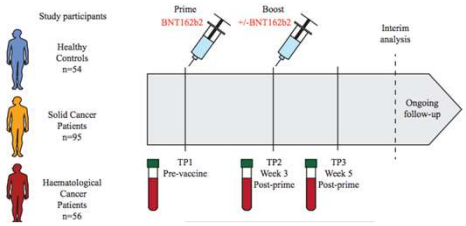
Clinical Efficacy and Safety Data of COVID-19 Vaccines in Patients with Cancer

Safety and immunogenicity of one versus two doses of the COVID-19 vaccine BNT162b2 for patients with cancer: interim analysis of a prospective observational study

Leticia Monin*, Adam G Laing*, Miguel Muñoz-Ruiz*, Duncan R McKenzie*, Irene del Molino del Barrio*, Thanussuyah Alaguthurai*, Clara Domingo-Vila, Thomas S Hayday, Carl Graham, Jeffrey Seow, Sultan Abdul-Jawad, Shraddha Kamdar, Elizabeth Harvey-Jones, Rosalind Graham, Jack Cooper, Muhammad Khan, Jennifer Vidler, Helen Kakkassery, Shubhankar Sinha, Richard Davis, Liane Dupont, Isaac Francos Quijorna, Charlotte O'Brien-Gare, Puay Ling Lee, Josephine Eum, Maria Conde Poole, Magdalene Joseph, Daniel Davies, Yin Wu, Angela Swampillai, Bernard V North, Ana Montes, Mark Harries, Anne Rigg, James Spicer, Michael H Malim, Paul Fields, Piers Patten, Francesca Di Rosa, Sophie Papa, Timothy Tree, Katie J Doores, Adrian C Hayday*†, Sheeba Irshad*†

Monin L, et al. *Lancet Oncol.* 2021;22(6):765-778.

Methods



Monin L, et al. *Lancet Oncol.* 2021;22(6):765-778.

Anti-SARS-CoV-2 IgG Response

		Immunogenicity at Week 5 (95% CI)	
	First dose Immunogenicity at Week 3 (95% CI)	No Boost	Day 21 Boost
Healthy controls	32/34 (94%, 81-98)	18/21 (86%, 65-95)	12/12 (100%, 76-100)
Solid cancer cohort	21/56 (38%, 26-51)	10/33 (30%, 17-47)	18/19 (95%, 75-99)
Hematological cancers cohort	8/44 (18%, 10-32)	4/26 (11%, 4-25)	3/5* (60%, 2-88)

Data are n/N; % (95% CI). 95% CIs were calculated by the Wilson method. *Insufficient numbers for clinical interpretation.
Monin L, et al. *Lancet Oncol* 2021;22(6):765-778.

NCCN: Limitations to efficacy data

- Antibody testing
  - Level of antibodies to yield protection is unknown
  - Routine post-vaccine testing is not recommended by the FDA
  - Difficult to interpret post-vaccination phase
  - Testing for select situations i.e.) research
- T- cell responses may play a role in providing protection
- Outcomes data among fully vaccinated patients with cancer are not available

NCCN: Cancer and COVID-19 Vaccination. Version 5.0, January 4, 2022.

NCCN: Specific safety considerations for patients with cancer

- Inactive vaccines
- Short-term data in patients on immune checkpoint inhibitors "no new immune-related side-effects or exacerbation of existing immune-related side-effects were observed"
- More data needed for specific therapies
- Results so far promising

Waissengrin B, Agbarya A, Safadi E, et al. Lancet Oncol 2021;22:581-583.
NCCN: Cancer and COVID-19 Vaccination. Version 5.0, January 4, 2022.

NCCN: Post-vaccine thrombosis

- Reports of Thrombosis with Thrombocytopenia Syndrome (TTS) with J& J vaccine
- No specific associations of TTS caused by vaccine in patients in cancer
- Patients with cancer have baseline increase risk for thrombosis = best to select another vaccine

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NCCN: Post-vaccine lymphadenopathy and imaging studies in patients with cancer

- Abnormal Imaging Findings
  - Reactive lymphadenopathy
    - Reported in up to 16% of patients
    - Presents unilaterally
    - Lasts up to 6 weeks
    - Abnormal FDG uptake with PET scanning
  - Reported with mRNA (Pfizer and Moderna) vaccines
  - Has not been reported with the J & J vaccine
- Addressing the issue
  - Goal is to avoid unwarranted biopsies
  - Specifics of vaccine history needed for radiologists
    - Date of vaccines
    - Site of injection
- Breast Cancer
  - The Society of Breast Cancer Imaging recommends scheduling screening imaging 4 to 6 weeks following completion of vaccination
  - If history of breast cancer, administer vaccine in the contralateral arm
- Overall Recommendations
  - As long as delay won't affect patient outcomes, delay imaging 4-6 following COVID-19 vaccine
  - If scans cannot be delayed, carefully consider full clinical picture

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Special Considerations

Timing around other vaccines?

- COVID-19 vaccines and other vaccines may be administered without regard to timing
  - Vaccines can be administered simultaneously
  - Coadministration within 14 days also permitted
- Clinical trial parameters may be the exception to the above
  - May exclude or require modification of standard-of-care vaccines
  - Discuss plans for COVID-19 vaccine with clinical trial investigators

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Revaccination Following HCT or CAR T-Cell Therapy

- Major concern for loss of immunity provided by vaccines following HCT or engineered cellular therapy
  - Observed with several childhood vaccines
  - Necessitates revaccination
  - Worsened in setting of GVHD
  - Lymphodepletion prior to therapy attenuates post-therapy immune responses
- Current recommendations
  - From CDC, American Society for Transplantation and Cellular Therapy (ASTCT), and American Society of Hematology (ASH)
  - Repeat vaccination series starting 3 months post treatment
  - NCCN supports these recommendations

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Pre-exposure prophylaxis: Background

- Vaccination is a form of pre-exposure prophylaxis
- Immunocompromised develop inadequate immune responses to vaccine
- Vaccine (humeral and cellular host response) + Immunotherapy (protection independent of host response)

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Pre-exposure prophylaxis: Tixagevimab + cilgavimab (Evusheld®)

- Long-acting monoclonal antibody combination directed against the spike protein
- Data
  - Effective as prophylaxis in patients at risk for COVID-19 complications
  - 77% reduction in risk of COVID-19 with risk reduction maintained through 6 months post dosing
- Supply is limited at the time
- Indicated in adults and pediatric individuals (≥12 years of age weighing at least 40 kg) who have moderate to severe immune compromise and may not mount an adequate immune response to COVID-19 vaccination
- Not a substitute for vaccination
- Guidance for timing vaccination post Evusheld® is not available

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Final Thoughts

Key principles to COVID-19 vaccination in patients with cancer

- Receive vaccination as soon as eligible
  - Increased risk of morbidity and mortality from COVID-19
  - Increased risk of complication from COVID-19
- Safety concerns low and comparable to general population
- Efficacy may be decreased
  - Especially in hematologic malignancies
  - Vaccine strongly recommended for all (when eligible)
- Goal is to protect yourself and your community

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Learning Assessment Question 1:

Which of the following vaccination timing recommendation is correctly paired?

a) All patients with hematologic malignancies should be vaccinated as soon as possible
b) Patients undergoing surgery should be vaccinated with regard to surgery
c) Patients undergoing surgery can be vaccinated without regard to surgery

Learning Assessment Question 2:

All of the following are ways to avoid misdiagnoses from abnormal imaging findings resulting from vaccination **except**

a) Report thorough vaccination history to radiologist
b) If clinically feasible, delay imaging by 6 weeks from time of vaccination
c) Utilize J&J vaccine for patients with cancer who will likely require imaging

Learning Assessment Question 3:

Which of the following is true with regards to pre-exposure prophylaxis with Tixagevimab + Cilgavimab (Evusheld)?

a) Cannot and should not replace vaccination
b) Should be reserved for the most immunocompromised but can be used for less immunocompromised patients especially if the patient and/or physician insist
c) If Evusheld is administered, vaccination must be delayed by at least 90 days