

## **Inclusion of Individuals with Cancer on COVID-19 Vaccine Trials**

### **A Joint Position Statement from the American Society of Clinical Oncology and Friends of Cancer Research**

**Approved by the ASCO Board of Directors May 20, 2021**

#### **Overview**

The safety of patients with cancer is the highest priority for oncologists and health care teams providing cancer care. During the COVID-19 public health emergency, the American Society of Clinical Oncology (ASCO) has created, curated, and disseminated information to help the cancer community ensure that they are providing the best possible cancer care to their patients during a time of great uncertainty and restrictions. Additionally, Friends of Cancer Research (*Friends*) has led collaborative efforts to gather data, share insights, and answer key questions to inform the collective COVID-19 response. There has been great progress, with multiple vaccines against COVID-19 authorized for emergency use by the FDA and other regulatory agencies, and vaccination campaigns are ongoing in the United States as well as other countries. Because patients with cancer were drastically under-represented on the clinical trials to evaluate the safety and efficacy of the rapidly developed COVID-19 vaccines, however, the vaccine safety and efficacy outcomes for patients with various types of cancer are not optimally characterized regarding safety, efficacy, and antibody responses.<sup>1</sup> Recommendations for vaccination of patients with cancer, particularly those undergoing active anticancer treatment, are currently based on consensus expert opinion in the absence of clinical evidence, while awaiting development of evidence from several ongoing studies that can provide more specific insights and guidance about populations with cancer.

Based upon real-world evidence in individuals with cancer (especially those with suppressed immune function), CDC guidelines include cancer as a high-risk medical condition that predisposes patients to severe illness from COVID-19.<sup>2,3,4,5</sup> Accordingly, ASCO, ESMO (the European Society for Medical Oncology), and other oncology professional organizations recommend vaccination unless specifically contraindicated. Patients with cancer often are discouraged from receiving vaccines that use live viruses because of potential risk of viral transmission with subsequent infection in those with compromised immune function. However, none of the currently approved COVID-19 vaccines contain live viruses. Insufficient evidence exists for understanding the degree of immunity to COVID-19 following vaccination in an individual with a compromised immune system, including those receiving chemotherapy. Patients with cancer who are vaccinated are encouraged to continue

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<sup>1</sup> Corti C, Crimini E, Tarantino P, et al: SARS-CoV-2 vaccines for cancer patients: a call to action. *European journal of cancer*. 148:316-327, 2021

<sup>2</sup> Centers for Disease Control: COVID-19: People with Certain Medical Conditions, 3/29/21 update. <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html>

<sup>3</sup> Kuderer NM, Choueiri TK, Shah DP, et al: Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *The Lancet* 395:1907-1918, 2020

<sup>4</sup> Izcovich A, Ragusa MA, Tortosa F, et al: Prognostic factors for severity and mortality in patients infected with COVID-19: A systematic review. *PLoS One* 15:e0241955, 2020

<sup>5</sup> Ganatra S, Dani SS, Redd R, et al: Outcomes of COVID-19 in Patients With a History of Cancer and Comorbid Cardiovascular Disease.1, 2020

to follow all guidance on masking and physical distancing to reduce any potential exposure to SARS-CoV-2.

As vaccination progresses worldwide, research is expanding to address questions such as the need for booster shots and variant-specific vaccines. Additionally, trials for specific subpopulations (e.g., pregnant women, children, immunocompromised patients) are underway or in the final planning stages. As more studies address special populations, it is critically important as part of vaccine development to study adequate numbers of patients who have cancer, have a suppressed immune system, or who are on immune-modulating treatments, to better understand the degree of immune response in this vulnerable population. This position statement aligns with recently published work from ASCO and *Friends* related to broadening eligibility criteria for safely increasing participation and inclusivity in cancer clinical trials.

## **Background**

There were an estimated 19 million new cancer cases worldwide in 2020 and nearly 1.9 million new cancer cases will be diagnosed in the U.S. in 2021.<sup>6,7</sup> Individuals with cancer are uniquely vulnerable to severe illness, hospitalization, or death due to COVID-19. It is imperative to better characterize the efficacy of COVID-19 vaccines for patients across the cancer continuum due to the unique impact of cancer diagnosis, age, and treatment-related immune function on COVID-19 infection. This increased risk makes specific vaccine safety and efficacy data critical for populations undergoing cancer treatment or with a history of cancer.

To date, clinical trials for COVID-19 vaccines have almost universally excluded patients receiving treatment for cancer, and many have excluded those who have a history of cancer, or those older than 65.<sup>8</sup> For example, some trial exclusion criteria incorporate: a history of cancer (except non-melanoma skin cancers), receipt of cytotoxic or immune-modulating treatment in the previous 6 months, and receipt of systemic corticosteroids.

The speed and success of global vaccine development programs for COVID-19 have been nothing short of incredible. Narrower, more homogenous patient populations may have been preferable in early-stage vaccine development to avoid compromising approval of potentially viable therapies. However, with multiple vaccines authorized for emergency use by the FDA and other national entities, as well as growing data on the safety profile of novel vaccines, eligibility should be expanded to include patients with cancer, a history of cancer, and cancer-related immunologic deficiencies.

Exclusion of patients with cancer from clinical trials without scientific justification (i.e., evidence of potential risk to patient safety) disproportionately impacts certain patient groups and patients with certain disease characteristics. Furthermore, lack of affirmative safety and efficacy data in patients with cancer compromises the ability to provide evidence-based counseling on the level of protection offered by COVID-19 vaccine in this vulnerable patient population. Therefore, unjustified exclusion compromises equity and inclusivity in addition to clinical decision-making.

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<sup>6</sup> International Agency for Research on Cancer (IARC): Estimated number of new cases in 2020, worldwide, both sexes, all ages. <https://gco.iarc.fr/today/online-analysis-table>

<sup>7</sup> American Cancer Society: Cancer Facts and Figures 2021, <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2021/cancer-facts-and-figures-2021.pdf>

<sup>8</sup> See NCT04324606, NCT04400838, NCT04536051, NCT04444674, NCT04405076, NCT04470427, and NCT04368728 at [clinicaltrials.gov](http://clinicaltrials.gov)

Recommendations by ASCO and Friends of Cancer Research assert that patients with cancer should be eligible for clinical trials as the default unless there is scientific justification for exclusion (i.e., evidence of potential risk to patient safety).<sup>9</sup> Additionally, eligibility criteria should evolve with growing clinical trial experience in a variety of populations to support the generalizability of results in different populations that may benefit. This principle should be currently applied to COVID-19 vaccine trials across the diversity of patients and spectrum of cancers.

### **Impact on Patients and Providers**

Safety risks associated with participation in vaccine trials will be unique to every patient with cancer. Patients with either a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of an investigational regimen should be eligible to enroll, per previous ASCO-*Friends* recommendations.<sup>10</sup>

Specific questions remain about optimal use of the COVID-19 vaccine in patients with cancer who are immune-suppressed or on immune-modulating treatment.<sup>11</sup> If there are specific concerns about immunogenicity and efficacy for a vaccine (e.g., in patients receiving chemotherapy, immunotherapy, CAR-T therapy, or transplants), priority consideration should be given for inclusion of cohorts of those patients in the prospective vaccine's trials. While oncologists are experienced in administering vaccines to their patients, specifics such as ideal timing between cycles of therapy, or length of waiting periods after stem cell transplants or immune globulin therapy, are not fully characterized for the COVID-19 vaccines. Should there be a clinically significant difference in response to the vaccine (including duration of efficacy) in patients with suppressed immune function, those data should be generated, appropriately analyzed, and disseminated as rapidly as possible. There are limited data on the response of patients with cancer to COVID-19 vaccines, but available results may indicate substantially improved response after the second dose of a two-dose regimen.<sup>12</sup> Efficacy and safety data for patients with cancer, or a history of cancer, receiving the COVID-19 vaccine regimen is needed. In addition, data on the impact of various therapies used in patients with cancer may influence response to the vaccine, and this information may help us better determine proper timing of vaccine administration.

### **Recommendations for Inclusion of Individuals with Cancer on COVID-19 Vaccine Trials**

- 1) Vaccine trial sponsors should design studies to be as broadly inclusive as possible. Existing and future COVID-19 vaccine trials should only exclude people with cancer (current or history of) and/or people who are immunocompromised if there is specific and credible risk of harm to them from trial participation.
- 2) Vaccine manufacturers and trial sponsors should prioritize recruitment of patients with cancer through partnerships with oncology practices, cancer centers, and academic medical centers. COVID-19 vaccine trials should be prospectively designed and purposefully recruit

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<sup>9</sup> Kim ES, Uldrick TS, Schenkel C, et al: Continuing to Broaden Eligibility Criteria to Make Clinical Trials More Representative and Inclusive: ASCO-Friends of Cancer Research Joint Research Statement. *Clinical Cancer Research*, 2021

<sup>10</sup> Lichtman SM, Harvey RD, Smit M-AD, et al: Modernizing Clinical Trial Eligibility Criteria: Recommendations of the American Society of Clinical Oncology-Friends of Cancer Research Organ Dysfunction, Prior or Concurrent Malignancy, and Comorbidities Working Group. *Journal of Clinical Oncology* 35:3753-3759, 2017

<sup>11</sup> See [https://www.nccn.org/covid-19/pdf/COVID-19\\_Vaccination\\_Guidance\\_V1.0.pdf](https://www.nccn.org/covid-19/pdf/COVID-19_Vaccination_Guidance_V1.0.pdf)

<sup>12</sup> Waissengrin B, Agbarya A, Safadi E, et al: Short-term safety of the BNT162b2 mRNA COVID-19 vaccine in patients with cancer treated with immune checkpoint inhibitors. *The Lancet Oncology*, 2021

sufficient numbers of individuals with cancer from diverse populations and age groups to enable valid subset analysis.

- 3) Government agencies with oversight of vaccine development and review should encourage and incentivize vaccine manufacturers to include patients with cancer in existing and future COVID-19 vaccine trials.
- 4) Public health agencies and other research organizations should design, collect, and analyze real world data on vaccine effectiveness in patients with cancer, in addition to clinical research data. For populations underrepresented in prior vaccine trials, this data collection would enable the most comprehensive understanding of practical clinical considerations.

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