Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Cancer Cell

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Letter

Care without a compass: Including patients with cancer in COVID-19 studies

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As the world enters the second year of the COVID-19 pandemic, the scientific community has generated essential data at a rapid pace to guide public health and therapeutic strategies. However, many of these efforts did not include a sizeable and vulnerable population: individuals living with cancer or with a history of cancer, a condition that across the globe affects 1 in 5 adults over a lifetime.

The available data on incidence, disease severity, and mortality of COVID-19 among individuals with cancer point to a higher burden of illness and adverse outcome rate among this population. In one of the largest observational studies focused on patients with both COVID-19 and a cancer diagnosis, our COVID-19 and Cancer Consortium (https://ccc19.org/) reported that among 4,966 patients studied, 58% were hospitalized and 14% died within 30 days, a mortality rate far higher than that observed in the general population (Grivas et al., 2021). Recipients of stem cell transplants with COVID-19 may face even higher mortality (Sharma et al., 2021). Claims- and electronic health record-based studies have consistently identified cancer as a leading risk factor for worse COVID-19 outcomes (Bakouny et al., 2020; https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html).

The accelerated development, testing, and regulatory authority for safe and highly effective vaccines to mitigate SARS-CoV-2 infection is a public health triumph. Yet the pivotal trials for the BNT162b2 (Pfizer/BioNTech), mRNA-1273 (Moderna), and Ad26.COV2.S (Janssen) vaccines excluded individuals with current or planned receipt of immune-suppressive therapy and, in some cases, those with a cancer diagnosed in the past 10 years. While the Pfizer/BioNTech trial did include 1,395 patients with a cancer diagnosis, these patients comprised only 3.7% of the study sample and reported no additional data about concomitant anti-cancer therapies. Out of 43,783 participants, the Janssen trial included 226 patients with cancer and 79 patients who had received stem cell transplants. While complete data have not been reviewed by the United States Food and Drug Administration, the published ChAdOx1 nCoV-19 (Oxford/Astra Zeneca) vaccine trial excluded patients with a history of cancer (https://clinicaltrials.gov/ct2/show/NCT04444674).

Taken together, we lack robust data on the safety and effectiveness of these vaccines against SARS-CoV-2 among patients with cancer to inform clinical decision making, prioritization, and public health policy (Ribas et al., 2021). Instead, professional organizations such as the National Comprehensive Cancer Network and the European Society of Medical Oncology have issued guidance based primarily on expert opinion and anecdotal evidence (Desai et al., 2021). Often, patients with hematologic malignancies and recipients of hematopoietic stem cell or chimeric antigen receptor T cell therapies experience suboptimal vaccine effectiveness against infectious agents, resulting in customized vaccination schedules among these populations (Cordonnier et al., 2019). Apart from one study that examined short-term safety of the BNT162b2 vaccine in 134 evaluable adults with cancer, our understanding of safety and efficacy in the larger population of individuals with cancer is incomplete (Waissengrin et al., 2021).

Sparse data exist on the use and outcomes of investigational COVID-19 treatments among patients with cancer. The United Kingdom RECOVERY Collaborative Group has published several large studies that have evaluated multiple therapies for use in patients with COVID-19, including a study that showed a statistically significant survival benefit of dexamethasone versus usual care among hospitalized patients (Horby et al., 2021). Unfortunately, this trial did not measure cancer as a specific comorbidity, leaving unanswered the question of the efficacy and safety of this regimen in the setting of cancer. Our team, for example, did not show a statistically significant survival benefit from dexamethasone among a cohort of patients with both COVID-19 and cancer (Rivera et al., 2020). However, the number of patients receiving corticosteroids was small, and most patients received additional treatments. When considering the question of anticoagulation, findings from the pivotal INSPIRATION trial did not support the use of empirical intermediate-dose prophylactic anticoagulation among critically

ill patients with COVID-19. Cancer was not measured as a co-existing condition—despite well-known pro-thrombotic tendencies of a number of cancers, their treatments, and associated complications (INSPIRATION Investigators et al., 2021).

Many of the proposed COVID-19 treatments exert body systems effects that can be substantially altered in patients with cancer. As examples, hematologic malignancies and myelosuppressive regimens, with resulting cytopenias, may render many patients immunocompromised. Steroids are used routinely as pre-medications, in addition to primary, salvage, and palliative therapies for many tumors. Certain drug therapies and cancer types, such as multiple myeloma, lymphoma, and adenocarcinomas, are associated with coagulopathies that require prophylactic anticoagulation. These highly prevalent conditions and their clinical features can complicate the approach to patients with both COVID-19 and cancer, forcing clinicians to extrapolate data from study populations that differ substantially from the patients seeking their guidance.

The Centers for Disease Control and Prevention recently listed COVID-19 as the third leading cause of death in the United States in 2020—just behind cancer (https://www.cdc.gov/mmwr/volumes/70/wr/mm7014e1.htm?s_cid=mm7014e1_w). The scientific community should recognize the disproportionately higher risks of COVID-19 infection for individuals with cancer and pursue efforts to generate clinically actionable data. When considering the size and clinical vulnerability of the population of individuals with cancer, it is astonishing that the stakes are so high and the evidence so scant. Members of the COVID-19 and Cancer Consortium propose three recommendations to strengthen the evidence base for prevention, treatment, and overall management of patients with cancer during the COVID-19 pandemic:

First, investigators should refrain from excluding patients with cancer from COVID-19-related studies. This recommendation includes both observational studies and interventional clinical trials.

Second, researchers should collect information about cancer history, diagnosis, and stage, and cancer treatment in all studies, using established data collection protocols to assure comparability across studies.

Third, study teams should consider active cancer and cancer history as covariates in data analyses, or report results from participants with both COVID-19 and cancer in pre-planned or stratified subgroup analyses, especially among patients with immunosuppression.

Adoption of these recommendations, coupled with prompt and transparent data reporting, can enable clinicians to implement COVID-19 prevention, diagnosis, and treatment strategies that have been shown to be safe and effective for this large, high-risk patient population.

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