Recommendations for Testing and Treating Outpatient Cancer Patients in the Era of COVID-19

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Abstract

The clinical spectrum of COVID-19 is still not fully understood. Cancer patients are uniquely vulnerable to COVID-19 and many have been or will be infected. Although an unfortunate minority will die from the infection, most will recover. This poses a challenge in which clinicians must weigh the benefits of initiation or resumption of antineoplastic therapy against the risks that antineoplastic treatment may worsen outcomes related to COVID-19 infection. A recent study of 423 patients at our institution found that patients in active cancer treatment who develop COVID-19 infection did not fare any worse than other hospitalized patients yet guidance as to who requires testing prior to antineoplastic therapy and when to resume therapy post-COVID diagnosis remains unknown. Our institution, therefore, commissioned a task force to help create guidelines for treating oncologists using available published literature. The taskforce focused on the ambulatory care testing guidelines only, as all inpatients receiving antineoplastic therapy are tested for COVID-19 prior to hospital admission. The guidelines focus solely on the safety and well-being of the individual patient undergoing antineoplastic therapy and are not designed to address infection control issues.

Cancer patients are uniquely vulnerable to COVID-19[1-6]. Initiation or resumption of antineoplastic therapy (chemotherapy, targeted therapy, or immunotherapy) poses a serious challenge in which clinicians must weigh the benefits of therapy against the risks of worsening outcomes related to COVID-19. To that end, our institution commissioned a taskforce to guide oncologists using available data. The taskforce consisted of oncologists with expertise in a variety of cancer types as well as an infectious diseases specialist. Additionally, the group solicited the opinions of other members of the infectious diseases and oncology services at our institution and met frequently over the course of several weeks as emerging data became more available.

The biggest data set, that included 423 patients diagnosed with COVID-19 between March 10 and April 7, came from our own institution.[7] The most frequent cancer types included solid tumors such as breast, colorectal, and lung cancer. Lymphoma was the most common hematologic malignancy. Over half of the cases were metastatic solid tumors. Like other studies, age, race, cardiac disease, hypertension, and chronic kidney disease correlated with severe outcomes.[8,9] Overall, 39.7% were hospitalized for COVID-19, and 20.6% developed severe respiratory illness. About 9.5% had to be placed on a mechanical ventilator and 12.1% died. Cancer treatments, including chemotherapy and surgery, did not contribute to worse outcomes. Patients receiving immune checkpoint inhibitors were more likely to develop severe disease and require hospitalization, however, most of the patients receiving immune checkpoint inhibitors had lung cancer and these patients may have confounding effects from other factors that were not fully evaluable. Specifically, in lung cancer, there are global efforts to understand the observed effect of COVID-19.[10]

The taskforce sought to define two distinct questions regarding adults with cancer receiving antineoplastic therapy in the ambulatory setting. First, when is COVID-19 testing appropriate prior to antineoplastic therapy for an asymptomatic patient; and, second, when is it safe to reinitiate therapy in a patient who has had COVID-19.

The main dilemma facing the group was striking the correct balance between risks associated with delaying antineoplastic therapy and those associated with initiation of antineoplastic therapy in the setting of COVID-19. We recognized that, in order to keep the guidelines concise and easy to use, we would not be able to address all possible situations. The guidelines were, therefore, written as a general framework for oncologists to follow.

Our recommendations were based on the following data and considerations. First, the guidelines focus on the safety of the individual patient undergoing antineoplastic therapy and were not designed to address infection control issues. Second, the decision to start or reinitiate antineoplastic therapy should rely on COVID-19-related risks associated with antineoplastic therapy and not on the risks inherent to the underlying condition. Third, among patients with cancer, those with advanced age, hematologic or lung cancer have the highest risk for severe COVID-19[4-6,11]. However, data indicate that antineoplastic therapy itself does not increase the severity of COVID-19[5,6,12]. Fourth, although antineoplastic treatment itself does not appear to increase the severity of COVID-19, there was concern, based on the current understanding of the pathophysiology of COVID-19, for more severe or prolonged COVID-19 in patients receiving antineoplastic treatments associated with prolonged lymphocytopenia or hypogammaglobulinemia[5,13,14]. These types of treatments are most commonly administered in the setting of hematologic malignancies. Fifth, while testing for COVID-19 was already widely

available at the time these guidelines were considered, the group recognized that unnecessary testing could lead to a delay in administration of antineoplastic therapy. Additionally, unnecessary testing could increase the risk of acquisition of COVID-19, as additional trips to healthcare facilities could be required. Sixth, SARS-CoV-2 RNA can be detected for several weeks after initial infection but does not distinguish between active and resolved infection[15-17]. In patients with mild to moderate illness, replicating virus cannot be detected after the first week of illness[18,19]. Finally, the taskforce put specific thought into the question of testing patients with lung cancer. Primary lung cancer has emerged as a substantial risk factor for severe outcomes with COVID-19 [5,12]. However, treatment of lung cancer with cytotoxic chemotherapy or with checkpoint blockade does not appear to further increase this risk [12]. We therefore decided, for the purpose of these guidelines, to group lung cancer with other solid tumors.

Based upon these considerations, the taskforce made the following recommendations:

Testing for the asymptomatic patient without a history of COVID-19

The taskforce recommended that only patients with hematologic malignancies should be tested for COVID-19 RNA prior to the initiation (i.e. on their first cycle) of outpatient antineoplastic therapy[4,5]. Routine pre-treatment COVID-19 RNA testing was not recommended for patients with solid tumors[5].

Resuming antineoplastic treatment therapy in a patient who previously tested positive for COVID-19 or who has had presumed recent COVID-19 infection.

The taskforce recommended that in a previously symptomatic patient with COVID-19, resumption of antineoplastic therapy be considered when COVID-related fevers have resolved for at least 7 days without use of fever-reducing medications, there has been a substantial improvement in respiratory symptoms, and at least 14 days have elapsed since onset of symptoms and/or initial positive COVID-19 test, whichever came earlier. Repeat COVID-19 RNA testing is not recommended[5]. In a previously asymptomatic patient with COVID-19, resumption of antineoplastic therapy can be considered when at least 14 days have elapsed since the initial positive COVID-19 test and no symptoms have developed during this time.

The taskforce recognized that certain patients may require additional time to recover prior to resumption of antineoplastic treatment. These include patients who experienced more severe symptoms due to COVID-19 (i.e. required hospitalization and/or supplemental oxygen), older patients[9,18], and patients with certain malignancies, such as lung cancer, hematologic malignancies[4,5]. Clinical discretion and the relative urgency of reinitiating cancer-directed therapy require consideration when using these guidelines.

Conclusions

In summary, we have put together guidelines to assist with the initiation of antineoplastic treatment in the setting of COVID-19. These guidelines were disseminated to all oncologists at our institution. While we recognize that these guidelines are based on the

current limited data and the opinions of their authors, we hope that they will be of use to physicians treating patients with cancer in other institutions.

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