Guest Editorial

Challenges to Treat Cancer Patients During COVID-19 Pandemic

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Introduction

The COVID-19 pandemic poses several challenges for oncology services. Providers must consider how to safeguard the morbidity and mortality of their patients as well as to minimize their patients' exposure to health-care facilities. We donot have a lot of data from published studies, but a report by Liang et al. provides the largest series consisting of 1,590 patients and describes the difference in outcome between cancer and non-cancer patients. In this model, which included adjustments for age, sex, and comorbidities, cancer was associated with an increased risk of death and/or intensive care unit admission (OR 5.4, 95% CI 1.8–16.2). These patients had a higher risk of severe events that required admittance to the intensive care unit, ventilation support, or that resulted in death.[1] However, caution should be taken with interpretation of this finding because the report included data from only 18 patients with cancer. So, despite being difficult to derive any conclusions from this report, it makes sense that people with cancer are at greater risk for being infected with the coronavirus as this virus is associated with the highest severity of illness in older people and those with comorbidities, such as heart disease, diabetes, and lung disease.

Clearly, there are potential risks associated with COVID-19. As oncologists, we are accustomed to dealing with infectious complications, but the challenge with COVID-19 is that there is no specific treatment available at the time. The risk-benefit ratio is tricky as on one hand, a patient might be at high risk of contracting COVID with potential fatality and on the other hand the patient might be at high risk of progression of cancer either leading to worsening of symptoms and even death if it is not treated timely and accordingly. Therefore, decision-making as a medical oncologist to assess whether initiate treatment for a newly diagnosed cancer patient or delay (and by how long) new treatment and for those already on treatment is a catch twenty-two.

Oncology societies and governmental authorities such as ESMO, ASCO, NCI and CDC have promptly issued guidelines on cancer care during this pandemic.[2–13] For example, the ESMO website includes general information on COVID-19, an FAQ section, and links to useful resources. All these guidelines have a common theme that oncologists remain vigilant and equip themselves with telemedicine services, reducing clinic visits, and switching to subcutaneous or oral therapies, when possible. There is also advice on supporting patients on infection control.

At Northwell Health, we continue to be one of the pioneer systems in adapting to this new world of medicine, with telephonic and telehealth consultations, modifying chemotherapy regimens to less frequent or reduced dose, conversion to oral chemotherapy or targeted agents, omitting more toxic agents especially those associated with severe myelosuppression or lung toxicity, using growth factors in high risk group, home delivery of oral medications including non-cancer repeat prescriptions, home collection of laboratory tests, port flushes, while some evaluations are being delayed. Of utmost importance, educating everybody about social distancing and the use of personal protective equipment amongst staff. Throughout our sites, we continue to provide lifesaving/prolonging chemotherapies, and either delaying or holding palliative or hormonal therapies which

require infusion center for indolent disease such as neuroendocrine tumors. With elective surgeries postponed, this further challenged us with treating selected group of patients during this pandemic. However, as the situation continues to evolve we continue to face difficult decisions but maintain the safety of our patients and staff. Another important point to be noticed here is that in addition to immunosuppression, many chemotherapy agents can also deteriorate other organ functions such as renal, hepatic, lung or cardiac. I cannot stress enough that individual patient decisions have to be made by multidisciplinary teams, who must discuss among each other and establish priority modality of treatment, either groups for surgery, systemic anticancer treatments, or radiotherapy.

Based on all my discussions and reviewing current CDC guidelines and NHCI previous newsletter, my recommendations for now would allow systemic chemotherapy after decisions based on the priority Table 1 adapted from National Health Service (NHS), UK as listed below[2]. This prioritization considers important factors, including the expected level of immunosuppression associated with individual cancer type and associated chemotherapy agent/regimen, treatments and cancer types, patient-specific risk factors for bothCOVID-19 and toxicity related to chemotherapy, assessing the risk and benefit that if cancer not being treated optimally with the risk of the patient being immunosuppressed and becoming seriously ill from COVID-19, and finally strongly keeping in mind medical resources, such as facilities, intensive care, equipment, workforce and other capacity issues.

Again, prioritization decisions are expected to be made as a result a multidisciplinary team by individualizing each patient‘s basis and recording the reasoning of this decision in the form of a medical documentation. It is also prudent to convey a clear message to patients and their care givers to understand prioritization and the reason for the decision to a particular patient is in alignment with safeguarding the patient, their families and staff. The lowest and highest priority categories are conceptual rather than

Table 1: *Level of Priority to Administer Chemotherapy During COVID-19 Pandemic*

Priority Level	Treatment	Disease Examples
1	• Curative treatment with a high (more than 50%) chance of success • Adjuvant or neoadjuvant treatment which adds at least 50% chance of cure to surgery or radiotherapy alone or treatment given at relapse	• Acute leukemias • Aggressive lymphomas • Germ cell tumors
2	• Curative treatment with an intermediate (20% – 50%) chance of success • Adjuvant or neoadjuvant treatment which adds 20% – 50% chance of cure to surgery or radiotherapy alone or treatment given at relapse	• Head and Neck • Anal cancer • Cervical cancer • Adjuvant chemotherapy for stage III colon cancer and high-risk breast cancer
3	• Curative treatment with a low (10% – 20%) chance of success • Adjuvant or neoadjuvant treatment which adds 10% – 20% chance of cure to surgery radiotherapy alone or treatment given at relapse • Non-curative treatment with a high (more than 50%) chance of more than 1-year extension to life	• Neoadjuvant or adjuvant chemotherapy for bladder cancer, or adjuvant chemotherapy for NSCLC
4	• Curative treatment with a very low (0% – 10%) chance of success • Adjuvant or neoadjuvant treatment which adds less than 10% chance of cure to surgery or radiotherapy alone or treatment given at relapse • Non-curative treatment with an intermediate (15% – 50%) chance of more than 1-year extension to life	• Immunotherapy for melanoma, systemic therapy for metastatic breast cancer or metastatic colorectal cancer
5	• Non-curative treatment with a high (more than 50%) chance of palliation or temporary tumor control and less than 1 year expected extension to life	• Palliative chemotherapy for upper gastrointestinal cancers
6	• On curative treatment with an intermediate (15% – 50%) chance of palliation or temporary tumor control and less than 1 year expected extension to life	• Second-line and third-line palliative chemotherapy for many solid malignancies

prescriptive. Priority of indications within each category is also variable and subject to the underlying principles including the magnitude of treatment benefit, possible effects of treatment delays or interruptions on outcomes, patient-specific considerations and the availability of staff and resources to safely deliver treatment. I must advise that some patients or cancers listed in lower categories are subject to change/escalation as the COVID-19 pandemic evolves.

There are many simple alterations which can be adopted during the pandemic. Minimize gathering of patients in the waiting area by careful scheduling, encouraging patients not to arrive early and if

Table 2: *Current Recommendations Regarding Cancer Patients*

Patient Type	Treatment Decision	Practice Points	Other
Not known to have COVID-19	• Treat per your institutional guidelines balancing risk and benefit.	• Patients should attend appointments without any accompanying family members or caregivers.	• Follow the usual infectious diseases guiding principles
Patients known or suspected to have COVID-19	• Defer systemic chemotherapy until the patient has at least 1 negative test for COVID-19. • If no test is available, then patients should wait > 14 days following resolution of their symptoms AND be negative for SARS-CoV-2 by PCR nasal swab or patients should wait > 28 days following resolution of their symptoms, if repeat testing not available. • If the multidisciplinary team feels the treatment for cancer must start urgently then you can follow CDC recommendations that suggests waiting at least 72 hours after the symptoms have resolved but remember this pertains to non-cancer patients per CDC. • However, given that the absence of symptoms is not associated with a predictably low viral load, it is advisable to retest the patient once symptoms have resolved, and proceed with planned cancer therapies only if a negative result is obtained. • Due to significant false negative rates in first-generation test kits, two consecutive negative tests within a 48-hour period can be considered, if available. • Serological assays to identify SARS-CoV-2 antibodies have been developed but are not readily available yet.	• Please assess with a multidisciplinary team whether continuing systemic chemotherapy is needed for urgent control of the cancer such as a cancer that is rapidly progressing and the risk-benefit assessment favors proceeding with continuing systemic chemotherapy.	• It is unclear how long a delay after the infection has resolved may be necessary before initiating/restarting anti-cancer therapy. • Based on experiences in Europe, testing must be performed on patients with lung cancer.
Patients with symptoms of COVID-19 at presentation	• Screen and triage to assess whether they are known or suspected to have COVID-19, or have been in contact with someone with confirmed infection. • Please manage according to the severity of symptoms and comorbidities and immediately transfer the patient to an assigned isolated location for further assessment.	• Mild cases of COVID-19 can be managed conservatively as outpatient. • More severe cases may warrant a higher level of care. • It is a known fact that neutropenic sepsis following chemotherapy may present with fever and with or without respiratory symptoms.	• Be mindful that the use of systemic chemotherapy resulting in an immunocompromised condition may result in have atypical presentations of COVID-19. • Moreover, differentiating symptoms of COVID-19 from neutropenic sepsis and pneumonitis could throw a challenge at least in the initial manifestations.

possible calling or texting patients when staff are ready to examine or treat a patent while they are waiting in their car.

To further implement social distancing and reduce the risk of COVID-19, consider alternative regimens or schedules of systemic chemotherapies, modes of administration (subcutaneous vs. intravenous or oral), regimens that are shorter in duration, decreasing the frequency between dosages (e.g. administer immunotherapies 4 – 6x's weekly where possible instead of 2 – 3x's weekly. Finally, consider strategic use of locations, especially if one site has capacity to treat a COVID-19 with chemotherapy, or to minimize patient exposure and maximize resources. We also recommend to defer supportive therapies such as Densoumab, Zoledronic acid, etc. unless indicated for hypercalcemia. Most endocrine therapies do not suppress the immune system, and it is agreed upon that endocrine therapies can be continued.

These procedures will not be successful without the proper education and reassurance of patients and their families, while maintaining the morale of staff. Alternative communication methods such as telephone, telehealth, FaceTime, and Skype can be utilized to undertake education, monitoring patients and consenting as well. However, recording all those procedures must be undertaken timely.

The challenge of if and when to treat a COVID-19 positive or a symptomatic patient with systemic chemotherapy remains. Table 2 summarizes current recommendations regarding cancer patients. Testing for COVID-19 is not readily available at each site, and PCR-related tests require time before the results are available.

Last but not the least, it is extremely important to notice that the COVID-19 pandemic has resulted in changes of cancer care for many reasons, including sickness of the physicians. It is crucial to follow the general rules and regulations related to the transfer of between providers. Such records should contain details of all treatments, including summary of chemotherapy treatment given, surgery, radiation or any procedures as well as the pathology report to confirm the diagnosis of cancer and diagnostic data including radiological evaluations and blood tests. It is also prudent that we as physicians take a proactive approach to discuss goals of care and advanced care planning with patients, especially those with advanced cancer who may succumb to COVID-19.

In summary, the COVID-19 pandemic has placed cancer patients at a higher risk, probably less to a hypothetical coincidence and more to the unavailability of the qualified staff and hospital resources. The COVID-19 pandemic has shown to overwhelm health-system capacity in many developed countries, such as Italy. We as oncologist do fully understand that postponing chemotherapy or other modalities to treat cancer is associated with potential risk of progression, more symptoms, and complications (obstruction, etc.). However, these risks will need to be balanced against the risk and potential morbidity and mortality related to COVD-19 infection. We except that this unwelcomed experience during the COVID-19 pandemic will prove with time whether the strategies that we adapted have impacted the outcomes. Throughout the pandemic, besides the cancer treatment, the utmost need is to uphold the psychosocial health of the patients and our staff who are risking their lives daily to treat cancer patients.

Until the pandemic has ended, we have to rely upon the principles of safety, transparency and evidence-based piers of priority in individualizing patients balanced with other general risk factors. We are constantly observing the fluidity of the situation as the context may need to be modified based on the revised CDC guidelines, local conditions, staff capacity and other resources. Please forward any questions to Nancy or myself. We are heavily involved with system communications and can help address any concerns you may have. Thank you for your continued dedication to our patients and your flexibility during this challenging time.

References

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