COVID-19 in patients with cancer: managing a pandemic within a pandemic

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The coronavirus disease 2019 (COVID-19) pandemic has disrupted health care worldwide. Patients with cancer seem to be particularly susceptible to morbidities and mortality from this novel disease. No COVID-19-specific therapy currently seems to offer a survival benefit to this unique patient population. Furthermore, the global effects on routine cancer care will likely be felt for decades to come.

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Coronavirus disease 2019 (COVID-19), a respiratory tract infection caused by the severe acute respiratory syndrome coronavirus named SARS-CoV-2, initially emerged in China in late 2019. The rapid global spread of this novel virus led the WHO to declare a pandemic with >30,000,000 confirmed cases, 946,000 deaths and >21,000,000 recoveries reported as of 18 September 2020, according to the Johns Hopkins Coronavirus Resource Center.

Initial reports from Asia suggested that elderly patients with multiple comorbidities, specifically diabetes, hypertension and obesity were at an increased risk of developing severe COVID-19 following SARS-CoV-2 infection[1,2]. As data on these risks have evolved, evidence has increasingly shown that patients with cancer are indeed a particularly vulnerable group. However, the effects of various confounding factors, including an older than average patient population who often have underlying comorbidities including a suppressed immune system and/or a hypercoagulable state, have been difficult to separate from the effects of having cancer. Equally confusing to clinicians are the common presenting symptoms of SARS-CoV-2 including, dyspnoea, cough, fever, fatigue, dysgeusia and less commonly diarrhoea and/or a hyperinflammatory syndrome, which are all common presenting symptoms of both cancer and toxicities from cancer therapy. Furthermore, the radiographic dilemma of distinguishing between immune-checkpoint inhibitor-induced pneumonitis from that caused by SARS-CoV-2 infection and conflicting data on the effects of certain therapies, such as steroids, on patient outcomes has left clinicians with considerable angst on how best to help patients presenting with acute or worsening symptoms[3]. The first reports describing outcomes in patients with COVID-19 included less than a handful of patients with cancer in Asia[1,2]. However, within months of the pandemic entering North America and Europe, large data series have emerged on the devastating effects of the virus on this unique patient population[4–6].

The largest report from China included data from 13,077 patients with COVID-19, including 232 who also had cancer. These patients were found to have an increased risk of severe COVID-19 (defined as a respiratory rate ≥30 breaths per min, oxygen saturation of 93% or lower in a resting state, a ratio of arterial partial pressure of oxygen to oxygen concentration ≤300 mm Hg, or >50% lesion progression on lung imaging within 24–48 h) and death, with rates of 64% and 20% in patients with cancer compared with 32% and 11% in 518 statistically matched patients without cancer, respectively[7]. Data from this study suggesting that older age, higher ECOG performance status and more advanced stage disease are all associated with an increased risk of mortality have been confirmed in other series, including those limited to patients with cancer from a single country, city or hospital system within North America and Europe[4–6,8]. Male patients and those from ethnic minorities also appear to be more likely to be diagnosed with COVID-19 and to have worse outcomes[9]. Data have differed in terms of the effects of specific interventions, including chemotherapy, immunotherapy and surgery, on outcomes of patients diagnosed with COVID-19. Importantly, not all patients with cancer appear to have equal risks of mortality from COVID-19: patients with lung cancer and those with haematological malignancies appear to be particularly susceptible. Regrettably, no single therapy used to treat COVID-19 has emerged as beneficial to patients with cancer, and data from the COVID-19 & Cancer Consortium suggest that hydroxychloroquine in combination with any other agent is associated with an increased risk of mortality, while remdesivir might be beneficial. However, knowledge on both the optimal timing of drug administration in relation to

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the onset of symptoms and the severity of symptoms in patients at the time of drug administration is lacking. Equally despairing is that patients with cancer seem to be less likely to be admitted to the intensive care unit for escalation of care[4].

The implications of the pandemic for patients with cancer will likely be felt for years to come, with fear and trepidation that the improvements in cancer-related mortality achieved in the years prior to the pandemic will be offset by interruption in screening programmes and other aspects of cancer care. In a model proposed by Norman Sharpless of the US National Cancer Institute, a 1% increase in deaths from colorectal and breast cancer is predicted to occur over the next decade as a result of the disruption of cancer care caused by the pandemic[10]. This predicted increase in mortality does not take into account delays in discovery and progress as a result of cancer centres temporarily closing research laboratories and diverting resources to patient care, the temporary suspension of clinical trial enrolment both by companies and local institutions, and the fact that being willing to travel to a medical centre to receive treatment is imperative to both the delivery and improvement of patient care.

Notably, the effects of the pandemic on cancer care have not been entirely negative. The rapid evolution of national and global consortia in order to better understand the effects of COVID-19 on patients with cancer and the transformation of cancer care to more patient-centric models are strategies that can be carried forward to improve patient care. Moreover, the record-breaking pace at which clinical trials evaluating potential therapies to treat, as well as prevent, COVID-19 have been launched sets a new standard for the organization of future therapeutic trials. Several trials involving SARS-CoV-2 vaccines are currently underway and will hopefully mitigate the effects of the pandemic on our global community. Given that patients with cancer are not included in many of these trials, how they will ultimately respond to such preventive measures remains largely unknown. Viral mutations might also occur during transmission and spread, leading to forecasts that SARS-CoV-2 will forever remain a looming threat to the oncology community. What is crucial to remember is that cancer itself is a pandemic with >18,000,000 people diagnosed worldwide. Many societies, including ESMO and ASCO, are providing clinical recommendations for the management of patients with cancer during this challenging time, recognizing that continuing to treat our patients sagaciously is critical to our role as physicians and advocates in their care.

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Competing interests

L.H. has acted as a consultant of Amgen, AstraZeneca, EMD Serono, Incyte, Merck, Roche and Xcovery and has received research funding from Boehringer Ingelheim, Bristol Myers Squibb, and Xcovery. L.H. became a full time employee of AstraZeneca after submission of this manuscript. M.G. has acted as a consultant of AstraZeneca, Celgene, Daiichi Sankyo, Mirati and MSD International, has received speaker fess from AstraZeneca, Bristol Myers Squibb, Celgene, Eli Lilly, MSD International, Pfizer, Roche and Takeda and has served on the advisory boards of AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim Italia, Celgene, Daiichi Sankyo, Eli Lilly, Ignyta, Incyte, Inivata, Jansen Cilag, MedImmune, Mirati, MSD International, Novartis, Pfizer, Roche, Seattle Genetics and Takeda.

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Johns Hopkins Coronavirus Resource Center: https://coronavirus.jhu.edu/
The COVID-19 & Cancer Consortium: https://ccc19.org/