Letter to the Editor

Colorectal Cancer

Official French SARS-CoV-2 guidelines for cancer patients, a triage solution with precision medicine

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"It is imperative to prioritize patients benefiting most from treatment in order to minimize exposure to SARS-CoV-2"

First draft submitted: 11 May 2020; Accepted for publication: 19 May 2020; Published online: 20 June 2020

One of the early guidelines to protect cancer patients against the novel coronavirus (SARS-CoV-2) was developed in early March by the French High Council for Public Health at the request of the French Health Ministry. These guidelines were prepared by a representative group of medical oncologists and radiation oncologists, working in both academic and private practice. The results of this initiative were published by You *et al.* in *Lancet Oncology* on 25 March [1]. In addition to ethical and practical considerations for the management of cancer patients in the context of the COVID-19 pandemic, these official guidelines provide helpful recommendations [1]:

- To reduce patient exposure and to minimize the risk of COVID-19 by prioritizing those most likely to respond to treatment;
- To facilitate the optimal use of hospital resources by adjusting treatment schedules.

These are pressing issues currently facing oncologists and the timely publication of this guidance and its alignment with international organizations is greatly appreciated. Indeed, these guidelines are invaluable because of the particular risk SARS-CoV-2 poses to patients with cancer [2,3]. The available data demonstrating cancer patients' susceptibility to influenza before the emergence of SARS-CoV-2 suggest that for cancer patients infected with influenza, the risk of hospital admission for respiratory distress is four-times higher, and the risk of death is ten-times higher than patients without cancer [3]. These elevated risks have been confirmed by very recent Chinese data for cancer patients in the current pandemic, also published in *Lancet Oncology* [2]. The French guidelines thus, recommend the adjustment of dosing schedules of chemotherapy or radiotherapy to reduce the frequency of hospital admissions (e.g., every 3 weeks, rather than weekly administration or hypofractionated radiotherapy). These guidelines stress that patients with cancer are at high risk of severe and urgent clinical complications, and those patients with cancer and COVID-19 should discontinue systemic anticancer treatments until complete resolution of symptoms. For patients with cancer without COVID-19, hospital admission for in-patient cancer care should be minimized to reduce the risk of exposure [1]. Hence, to effectively implement these recommendations and help support physicians' decisions with accurate information on the patient's profile, practical solutions are welcome.

In April, Marshall *et al.* published in your journal their whitepaper outlining strategies to reduce COVID-19 risk and maintain treatment benefits in colorectal cancer (CRC) care, where the value of effective solutions for triage with innovative biomarkers was stressed [4]. CRC is a major healthcare burden in oncology. Based on our experience in this area at the Fleming Institute of Oncology (Buenos Aires, Argentina), we believe – like our colleagues from the Ruesch Oncology Center at Georgetown University (WA, USA) – that compliance to the guidelines during this crisis period and its aftermath could be significantly improved by using a practical and pragmatic solution offered by precision medicine in immune-oncology.

The WHO (Geneva, Switzerland) and the International Agency for Research on Cancer (Lyon, France) recommended the assessment for immune response in CRC tumor diagnosis in their 2019 pathology blue book [5]. The assessment on the tumor site is performed by generating an 'immunoscore' [6]. This score informs treatment

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decisions in stage II–III colon cancer by identifying those patients most likely to relapse or respond to shorter cycles of chemotherapy, without sacrificing benefit [7,8]. Similarly to Marshall *et al.* who outlined this de-escalation solution for SARS-CoV-2 and CRC treatment recommendations [4], we believe this tumor score is of considerable relevance given the current pandemic, as it documents patient triage decisions without adding specific pathology procedures and can be performed without any person-to-person contact. In our center we assessed several stage II and III patients using the immunoscore and were able to de-escalate treatment in half of these cases.

The process entails generating an immunoscore by digital pathology on resected tumor samples to identify local densities of $CD3^+$ and $CD8^+$ lymphocytes, which is correlated with the risk of recurrence [7]. Published in the *Lancet*, a society for immunotherapy of cancer (WI, USA), reported immunoscore to be robust, reproducible and capable of superior prediction of overall survival to existing parameters, such as microsatellite instability [7]. A subgroup analysis demonstrated that for high-risk stage II CRC patients with a high immunoscore, adjuvant chemotherapy should be avoided [4]. The IDEA-Fr trial determined that immunoscore may determine whether 3 months of adjuvant treatment in stage III colon cancer will be noninferior to 6 months' treatment [8]. Moreover, these qualities are in-line with the ESMO COVID-19 guidelines for prioritizing care in colon cancer [9].

It is imperative to prioritize patients benefiting most from treatment in order to minimize exposure to SARS-CoV-2. Based on our experience, we believe that determining the immunoscore in early-stage colon cancer is a practical way of implementing the French guidelines. Although this method is currently dedicated to colon cancer, it may inspire oncologists to prioritize precision medicine tools in other cancer types.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

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