Patients with cancer have been reported to be at higher risk for severe events and are associated with poorer outcomes after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)/coronavirus disease 2019 (COVID-19) infection than individuals without cancer. Cancer management requires frequent hospital visits and patient access for diagnostic procedures, treatment, and disease surveillance. These patients may be immunocompromised because of several conditions, including the underlying malignancy and anticancer treatments. This leads to a higher risk of developing infections, including SARS-CoV-2. Recently, hospital admissions and recurrent hospital visits have been reported as potential risk factors for COVID-19 infection.

To reduce the risk of infection and the number of clinic visits for patients with cancer, several different strategies have been proposed, including postponing/temporarily suspending ongoing treatments whenever possible (eg, adjuvant chemotherapy or elective surgery for less aggressive cancers), preferring oral therapies to intravenous agents and shorter radiotherapy fractionation, switching to regimens with longer intervals, increasing intervals between scans, and replacing clinic visits with teledmedicine tools and/or telephone appointments. Case-by-case evaluations of the risk/benefit ratio of delaying anticancer treatments are crucial. Delays in surgery for incidental cancers, for instance, have been shown to significantly affect the long-term survival of patients with cancer, with the health impact of delaying cancer surgery for 6 months being approximately 60% of the health gains of hospitalizations for community-acquired COVID-19 infection. Administering neoadjuvant or adjuvant chemotherapy regimens with suboptimal timing might negatively affect the outcomes of potentially cured patients. Furthermore, treatment delays and holds in patients with advanced disease might contribute to disease progression with a negative impact on patient survival and quality of life.

Tumor genotyping is an essential step in cancer management in most solid tumors. It allows for an optimized treatment strategy based on molecular findings and has been shown to improve significantly the outcomes of patients with cancer.

Liquid biopsy, namely cell-free DNA (cfDNA) analysis, has already entered clinical practice in advanced non–small cell lung cancer for epidermal growth factor receptor (EGFR) mutational testing and more recently for the identification of PI3KCA mutations in breast cancer. However, the indications are constantly growing, and the availability of several different commercially available plasma next-generation sequencing (NGS) platforms that simultaneously evaluate multiple genetic alterations (mutations, amplifications, and rearrangements) could extend liquid biopsy use to other settings and solid tumors. Robust evidence suggests that the integration of plasma NGS into the routine management of advanced cancers is associated with an increase in the detection of therapeutically targetable mutations, improves the delivery of molecularly guided therapies, and thereby rescues a significant proportion of apparently biomarker-negative patients. Furthermore, the use of plasma NGS could increase the identification of some emerging tumor-agnostic targets that have been recently added to the list of therapeutically exploitable oncogenes, such as RET and NTRK gene fusions.

The worries for nosocomial contagion of COVID-19 infection are significantly limiting access to diagnostic procedures and/or clinic visits essential for cancer diagnosis. This is demonstrated by a significant reduction of cancer diagnoses in comparison with the period before the COVID-19 outbreak, as recently reported in a recent analysis of the Netherlands Cancer Registry.

In this global health crisis, the use of minimally invasive tools might be extremely useful for reducing the potential risks of contagion for patients with cancer by limiting clinic visits or hospitalizations for patients with insufficient/unavailable tissue for tumor genotyping. Furthermore, implementation of plasma NGS concomitantly with tissue testing...
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Can increase the detection rate up to 26% more clinically relevant biomarkers in most solid tumors. This would extend the number of patients potentially treated with targeted agents and protect patients from additional exposure in an infusion clinic because most of these targeted agents are orally administered. The use of liquid biopsy “first” could also reduce the time to treatment start for tumors for which complete tumor genotyping is essential for appropriate cancer management, such as non–small cell lung cancer, because of a lower turnaround time in comparison with tissue testing, and this could prevent further delays in treatment start for patients who have experienced significant delays during the diagnostic workup because of this health crisis. We propose, therefore, a shift in the current diagnostic workflow for patients with metastatic cancer to incorporate the use of liquid biopsy. This could be implemented via home phlebotomy services, retail clinics in pharmacies, and/or mobile units for blood draws, all followed by a central NGS analysis of cfDNA. The reports are transmitted online, and therapeutic decisions are made on the basis of evidence-based tools for interpreting the actionability of molecular alterations (eg, the ESMO Scale for Clinical Actionability of Molecular Targets and OncoKB) in the context of a multidisciplinary molecular tumor board (Fig. 1). This proposal, born in the time of a severe crisis for the health care system, might also be applied when the SARS-CoV-2 outbreak ends and thereby reduce the turnaround time for results from molecular testing for patients with cancer and increase the number of patients potentially benefiting from highly effective targeted therapies.

Finally, recent studies have hypothesized the use of cfDNA as a monitoring tool during anticancer therapies, including targeted therapies for oncogene-addicted tumors and immune checkpoint inhibitors. This emerging application for liquid biopsy could be particularly useful during the SARS-CoV-2 outbreak not only in clinical practice but also in clinical trials. The performance of oncology clinical trials has been deeply affected during the SARS-CoV-2 pandemic, and the changes dictated by this novel clinical situation could prompt the development of more efficient and streamlined methods of trial conduct and data collection in the near future. In this scenario, liquid biopsy could play an important role by changing dramatically the way that we are used to conducting clinical trials.

It is time to move on from our current clinical practice and extend the use liquid biopsy to broader clinical applications.

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