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► **To cite this version:**

Bertrand Routy, Lisa Derosa, Laurence Zitvogel, Guido Kroemer. COVID-19: a challenge for oncology services. *OncoImmunology*, 2020, 9 (1), 10.1080/2162402X.2020.1760686 . hal-03150177

HAL Id: hal-03150177

<https://amu.hal.science/hal-03150177v1>

Submitted on 13 Nov 2024

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COVID-19: a challenge for oncology services

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On March 11, 2020, the WHO declared that the cluster of pneumonia cases caused by the novel coronavirus SARS-CoV-2 (COVID-19) from Wuhan, China was a global pandemic.¹ As of April 5th 2020, over to 1.2 million cases have been reported worldwide, with over 65,000 deaths (source: WHO website), knowing that both values are certainly underestimated.

Thus far, risk factors of COVID-19-related complications or fatal outcome are known to include advanced age (>70 years) and comorbidities such as preexisting respiratory, cardiac diseases, hypertension, and obesity.^{2,3} Patients living with cancer are at particularly high risk due to immunosuppression caused by both malignancy and anticancer treatments. Liang et al. were the first to describe a nation-wide analysis in China of COVID-19 cases in patients with a history of cancer.⁴ Out of 1590 identified cases of COVID-19, 18 patients had a history of malignant disease, with lung cancer being the most frequent type of neoplasia. One quarter of these patients had received either chemotherapy or surgery during the month prior to diagnosis. The patients with cancer identified in this study were more likely to experience severe disease (with a higher risk of ICU-admission, invasive ventilation, and death), particularly those who received anti-cancer therapy in the month prior to COVID-19 diagnosis. Similarly, an Italian group reported that, among a COVID-19-positive population of 355 patients who succumbed to COVID-19 at the time of the publication, 20.3% had active cancer.⁵

Amid the rapidly growing number of COVID-19 cases worldwide that have led to unprecedented stress on the health care system, cancer patients are also at a higher risk of not receiving planned treatment. To continue to provide care to oncological patients, prevention measures should immediately be implemented to protect cancer patients, health care professionals and maintain cancer units as COVID-free zones.

1. Outpatient management

As cancer patients are especially susceptible to COVID-19 infection, their visits to the hospital should be kept to a minimum and limited to treatment. In addition, to encourage strict confinement

measures for patients, the following actions to decrease medical visits, invasive procedures and imaging should be considered.

First, telemedicine through web based-applications or via telephone represents a safe approach to assess patients regularly on a regular basis.⁶ In our experience, up to 85% of regular follow-ups can be replaced by a telephone call.

Second, a careful balance between the risk of delaying a treatment *versus* the risk of COVID-19 infection should be addressed. For non-indolent cancers, a delay of 3 months potentially represents the best alternative.⁷ However, if the treatment cannot be postponed or has already been initiated, alternative dosing should be considered. Indeed, for immune checkpoint inhibitors, strong pharmacological data demonstrated similar efficacy of anti-PD-1 Abs infused every 6 weeks compared to every 3 weeks.⁸ In addition, the role of maintenance therapy should be reconsidered in patients with long-lasting stable disease or in remission. For radiotherapy, curative hypofractionated treatment should be recommended.⁹ For each tumor site, more precise expert resources and guidance are available on the websites of the American Society of Clinical Oncology, European Society Medical Oncology and American Society of Hematology.

Unfortunately, in light of the unrelenting strain placed upon the health care system and the reassignment of medical teams to COVID-19-specific units, oncologists also need to base their clinical decisions on the impact of their treatments on the outcome. For example, treatments with limited impact on overall survival (such as adjuvant chemotherapy in node-negative non-small-cell lung carcinoma) or therapies that improve prognosis by only a few weeks or months should not be administered. In addition, patients over the age of 70 years are at extremely high risk of developing severe COVID-19,³ suggesting that oncological treatments (for non-curative intent) should be carefully evaluated for their true utility.

Third, chemotherapy units must remain a COVID-free sanctuary. Prior to receiving treatment, telephone screening of patients should be mandatory. In the presence of symptoms, patients should be investigated thoroughly. Patients should receive their treatment without being accompanied

by any family members to decrease the risk of contamination. Furthermore, to protect these units, medical staff assigned to treatment infusion and management of toxicities should be prohibited from working in other COVID-associated wards, whenever possible. (Figure 1)

Fourth, as to follow-up exams, only important CT or PET scans that will change the clinical management/treatment should be performed. Efforts should focus on delaying non-urgent imaging and decreasing hospital visits.

2. Inpatient management

Unavoidably, some patients will need to be admitted to the hospital for therapeutic complications or inpatient treatments. It is imperative that the hemato-oncology wards remain COVID-free, and that all patients undergo a thorough screening process before they are admitted in these units. Medical personnel including orderlies, nurses, pharmacists and physicians, should be exclusively assigned to these units and should not be in contact with COVID-19 positive patients. Indications for autologous and allogeneic stem cell transplantations should be reconsidered and discussed during virtual tumor board meetings. Only urgent transplants with curative intent should be offered to patients.

For patients that are already hospitalized, a systematic screening (that is not limited to suspected cases of COVID-19 but includes all patients) should confirm the absence of COVID-19. Cancer patients who test positive for COVID-19 must be treated in a dedicated COVID-19 unit that is kept separate, with distinct personnel engaged in the use of personal protective equipment and strict infection prevention measures. It will be important to treat COVID-19 patients as soon as they are positive (even before they develop any symptoms of the infection) using under medical supervision agents that

target viral enzymes (such as favipiravir) or host cells (such as hydroxychloroquine plus azithromycin) to reduce viral replication. Although these treatments have not been evaluated in Phase III clinical trials, at this point it appears a moral obligation to attempt experimental treatments rather than to passively await the results of such trials.

Finally, even the asymptomatic medical staff should be systematically tested for the presence of oropharyngeal COVID-19 on a weekly basis.

3. Clinical trials

To protect medical personnel and provide support to COVID-19-specific units, most ongoing oncology clinical trials have been temporarily stopped.¹⁰ The COVID-19 pandemic has driven unprecedented research efforts in finding treatments and vaccines, and has galvanized the medical and research community to cooperate and to share data on high-risk individuals (and hence to create a COVID-19 cancer registry) and clinical observations (such as the impact of immunotherapy on COVID-19) in order to improve patient management.

4. Unmet research needs

It will be important to find out i) novel diagnostics to stratify COVID-19 patients not only based on viral load and virulence, but also according to their status of inflammation or immunosuppression, or in contrast their immune activation (humoral and cellular immune responses), ii) which type of cancer therapy favors (or attenuates) the susceptibility to severe COVID-19, in particular the effects of PD-1/PD-L1-targeting immunotherapy on COVID-19, iii) whether experimental or clinically approved

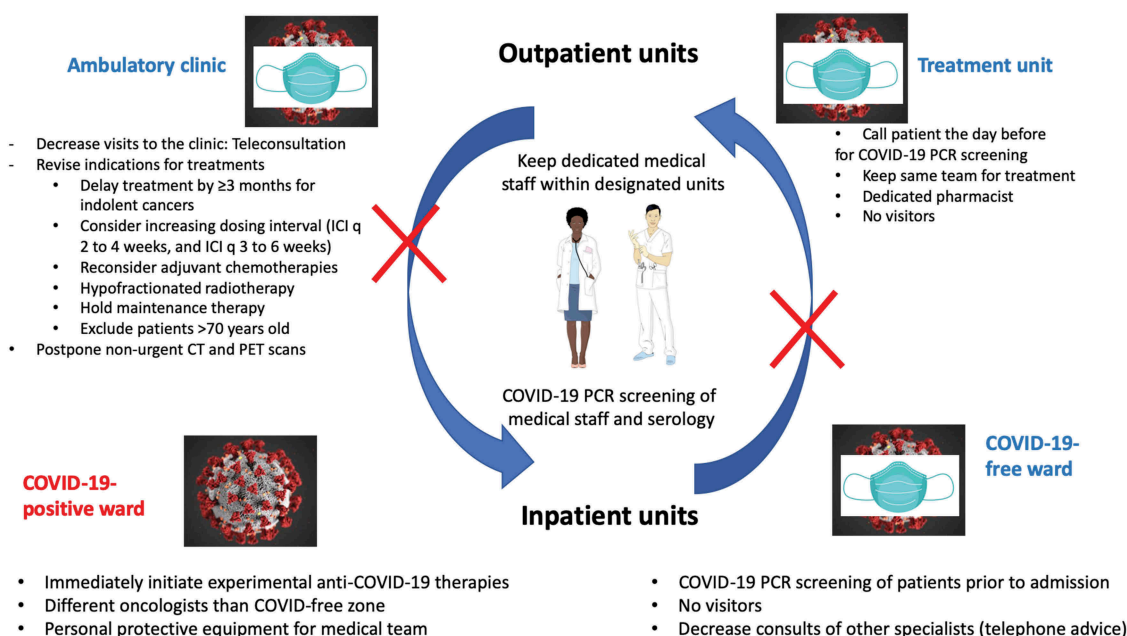


Figure 1. Reorganization of oncology services during the COVID-19 pandemic. ICI: Immune checkpoint inhibitors.

anti-COVID-19 medications interfere with the efficacy of anticancer immunotherapies.

In summary, the current COVID-19 outbreak requires a reorganization of cancer care and oncological wards at multiple levels, imposing a series of difficult choices to optimize a health care system that is under stress. Several European and Canadian COVID-19 cancer consortia are following the Chinese efforts including <https://ccc19.org> and ONCOVID trial (NCT04341207) at Gustave Roussy and across multiple cancer centers. In this pandemic setting, innovative approaches to maintain safe follow-ups and treatments are needed.

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