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Cancer, The Patient and The Oncologist during the COVID-19 Pandemic

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Introduction

Since world cancer day this past February 4th, 2020, the world has witnessed the most extraordinary health challenge for a generation. The coronavirus pandemic has changed the way we live, work, and interacts with each other, probably forever.

Governments around the world have called on their citizens to take personal and collective responsibility for the health of themselves, their families, friends, colleagues and neighbors. This call to action will help limit the spread of the virus and save lives.

The global cancer community understands that we are stronger when we act together. For two decades we have come together to raise the profile of cancer, embodied in world cancer day.

Hundreds of thousands, if not millions of people have come together in towns, cities and countries to raise awareness and act against a disease that kills millions each year. This same opportunity for solidarity is evident now as we join the global response to the coronavirus.

People living with cancer, their families, and those who support and care for them have a double burden: avoiding a virus as well as continuing life-saving cancer treatment. We salute all who are sailing on this very difficult and disturbing journey around the world.

The spirit of our cancer community shone on February 4th, 2020 as the pandemic progressed worldwide. We think twice before sharing the annual reports on the Impact of the encouraging data on World Cancer Day at a time when the world feels more anxious and uncertain.

However, I think it is important, perhaps now more than ever, to highlight the spirit and energy of the international community fighting cancer and to synthesize some relevant points of care for cancer patients and the oncologists who assist them.

Caring for the health of others and the most vulnerable for us is part of our DNA, and these reports bring to life that spirit of hope that is serving communities everywhere today. We may be socially estranged but being apart does not mean that we must go through this journey alone. The passion to help unites us and will be what takes us all forward.

Thanks to the cancer community for the tireless work they do. Your commitment, perseverance and optimism are what we need at this difficult time.

Vision of the Sanitary Problem

On March 11th, 2020, the World Health Organization (WHO) took the step it had been avoiding for weeks and declared that the spread of the 2019 Coronavirus Disease (COVID-19) and the virus causing it, now identified as SARS-CoV-2, had reached global levels of pandemic, the first pandemic caused by a coronavirus. The WHO has not declared a global pandemic since 2009, when it gave that designation to a new strain of H1N1 influenza. "The WHO has been evaluating this outbreak throughout the day, and we are deeply concerned, both by the alarming levels of spread and severity and by the alarming levels of inaction," said WHO Director-General Tedros Adhanom Ghebreyesus, PhD, MSc, during a press conference announcing the change in the WHO assessment of the coronavirus outbreak from epidemic to pandemic. "We rang the alarm bell loud and clear".

According to the WHO, in just 2 weeks, the number of COVID-19 cases outside of China, where the outbreak was first identified in December 2019, increased 13-fold to more than 118,000 cases worldwide, with 4,300 deaths, and the number of countries affected had tripled to 114 [1].

But the scope of the outbreak is increasing at a high speed, updated data compiled by the Johns

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Hopkins University Center for Science and Systems Engineering (CSSE) finds that the global spread of the coronavirus, as of March 19th, 2020, has reached 222,642 cases and resulted in 9,115 deaths in 159 countries. At the time of writing this note, the information speaks of 2,000,000 infected and more than 128,000 deaths worldwide. (Wednesday, April 15th, 2020, 1:00 p.m.).

In the United States, the new coronavirus has infected more than half a million people in all 50 states and the District of Columbia, with the majority of outbreaks grouped in Washington state, New York, and California, and has resulted in al minus 27,000 deaths, according to CSSE.

But these numbers are expected to skyrocket to tens of thousands and even millions as more people undergo coronavirus screening.

To help curb the spread of the virus, a new guide from the Centers for Disease Control and Prevention is calling for public meetings to be limited to 10 people in the next 15 days. (For daily updates on the global spread of COVID-19, visit the CSSE website.)

Protection of Doctors, Paramedical Personnel and Patients

The dizzying rate of disease spread has caused coronavirus response efforts to shift from containment to mitigation strategies to reduce the public's risk of contracting the virus, including calls to isolate sick people at home; closure of schools, bars, restaurants and cinemas; and encourage teleworking. In the US, President Donald Trump (who initially denied the severity of the Pandemic) instituted a 30-day travel ban from 26 European countries to the United States beginning March 13; public gatherings across the country were discouraged and even banned in many places; and major medical conferences, festivals, and sporting events in the United States and around the world are being cancelled or postponed as the coronavirus continues to spread. In the cancer community, the response has been swift to protect doctors and paramedical personnel and cancer patients, who may be especially vulnerable to contracting the coronavirus due to their systemic immunosuppressive status caused by their disease and cancer treatments, including chemotherapy, biological treatments, immunotherapy, radiotherapy and surgery.

We don't have much data from published studies yet, but an analysis of a small Chinese study of 2,007 cases of COVID-19 found that 18 cases had a history of cancer. These patients were at increased risk for serious events requiring admission to the intensive care unit, ventilation assistance, or death.

Because the number of cancer patients in this study is so small, it is difficult to draw real conclusions from the findings, but since the virus appears to cause the greatest severity of the disease in older people and people with comorbidities, such as diseases Heart disease, diabetes, and lung disease, it makes sense that people with cancer have an increased risk of becoming infected with the coronavirus.

To reduce the risk of infection for patients and staff members, various cancer institutions, such as the University of Texas MD Anderson Cancer Center in Houston, Memorial Sloan Kettering Cancer Center in New York, and Dana-Farber Cancer Institute in Boston, they have cancelled all work related travel for meetings or conferences. At Mount Sinai Hospital, patients on active cancer treatment receive a phone call or text message before their appointment, asking about their health and any symptoms of the virus they may be experiencing, such as coughing and shortness of breath.

When he writes this, speaking recently with a colleague from the USA, Chief of Oncohematology at a major hospital in the city of Hollywood, Florida, he said to me ... "I ask my patients in active treatment to stay at home as long as possible and practice social distancing to reduce exposure to the virus. We have also cancelled the activity of cancer support groups at the hospital and are instead connecting patients by teleconference or by phone so that they can access support groups, but not in person."

Currently, the criteria is to reschedule routine follow-up appointments for cancer patients who have completed active treatment until at least May/June to further limit the risk of infection for patients and staff in the hospital, and/or private practice.

The Difficulty of Stopping the Spread of the Coronavirus

Although much is still unknown about this new strain of coronavirus, including how easily it spreads, according to the CDC, based on what is currently known about COVID-19 and other coronaviruses, the spread is generally believed to occur from one person to another through respiratory droplets from close contact with a person infected with the virus, although spread can also occur from contact with infected surfaces or objects. Researchers are beginning to collect some key epidemiological characteristics of the virus, which could have important public safety implications to mitigate the spread of the virus.

According to a recent Lauer study investigating the estimated length of the COVID-19 incubation period, evidence suggests that the average incubation period is approximately 5 days, which is similar to that of severe acute respiratory syndrome, and that patients should expect to experience symptoms within 12 days. The study results support current CDC recommendations to actively monitor patients for 14 days after exposure to the virus. However, although people infected with the coronavirus are believed to be more contagious when they have symptoms, such as fever, body aches, cough, runny nose, sore throat, and difficulty breathing, cases of spread of the coronavirus have been reported before people develop symptoms. The fact that people who are asymptomatic or have only mild symptoms can transmit the virus makes it particularly difficult to control the spread.

Oncology Medication Missing?

Also of concern is the effect of the coronavirus outbreak on drug shortages, as pharmaceutical supply chains in China, the second largest exporter of drugs after India, and biological products or drugs of natural origin, to the world they can be interrupted by the outbreak. In our country, for the moment, no official information has been reported (Ministry of Health, ANMAT, Scientific Societies, etc.) that there is a lack of antitumor drugs.

The Patient

Who is at specific risk?

So far, there are no scientific evidence-based reports available on an increased incidence of asymptomatic COVID-19 or SARS-CoV2 infections in cancer patients. However, recent limited data from China, and more recently from Italy and the United States, seem to confirm an increased risk.

Available data indicates that older people are more vulnerable, with underlying health conditions such as chronic respiratory,

cardiovascular, or chronic kidney disease, diabetes, active cancer, and generally serious chronic disease. Therefore, during the COVID-19 pandemic, the relationship benefit/risk of cancer treatment may need to be reconsidered in certain patients.

Two groups of patients have been identified: "patients without therapy" (A) who have completed a treatment or have the disease under control (without therapy); and patients in treatment (neoadjuvant or adjuvant curative treatment or treatment for metastatic disease) (B). Patients with "active disease" may be eligible for surgery, chemotherapy and/or radiation therapy, biological therapy, endocrine therapy, and immunotherapy (either in the adjuvant or in the metastatic setting). For all patients (A and B) it is mandatory to provide health education: a) Avoid crowded places; b) Wear "masks" or chinstraps when you go to the hospital for visits and treatments; c) wash your hands correctly according to the instructions of the World Health Organization (WHO); d) Not having contacts with friends and family with symptoms of COVID-19 or who live in endemic areas; e) Guarantee social distancing with all people: Protect yourself to protect others.

For patients receiving active treatment (B), whether or not they live in epidemic areas, hospitals should identify specific pathways to ensure the timing of treatment with curative intent and, where possible, also for patients with metastatic disease.

Outpatient visits for cancer patients should be reduced to the safest and most feasible level without jeopardizing patient care. For patients receiving oral treatment for whom monitoring can be done remotely, provision of medication for at least 3 courses should be provided to reduce access to the hospital.

Blood monitoring for these patients can be done in local laboratories near home. We suggest the implementation of telemedicine services. We recommend delaying all follow-up visits. More intensive surveillance should be used during treatment for patients with lung cancer or who received prior lung surgery, and for older patients or those with other comorbidities. Intensive measures must be taken to prevent intra-hospital spread.

There should be strict and safe evaluation procedures to evaluate any symptoms of COVID-19 and the urgency and need for hospitalization. In order to regulate access to "Cancer Centers", establish the detection of "checkpoint areas" for the early detection of potentially infectious people. Clinical staff responsible for the checkpoint area should be trained and wear masks. People who meet the criteria for highly communicable diseases that require isolation, such as the new COVID-19 or other emerging infections, should be placed in a private exam room as soon as possible, according to the infectious control guide posted on the sites WHO and CDC website. They must be tested and transferred to dedicated areas of COVID-19.

In Cancer Patients, The Categories at Risk Include

- Patients receiving chemotherapy or who have received chemotherapy in the last 3 months.
- Patients receiving radiotherapy
- People who have had bone marrow or stem cell transplants in the past 6 months, or who are still taking immunosuppressive medications.
- People with some types of cancer of the blood or lymphatic system that damage the immune system, even if they have not needed treatment (for example, chronic leukemia, lymphoma, or myeloma).

Specific Risk Groups are Cancer Patients with an Impaired Immune System such as

- Leukocytopenia
- Low immunoglobulin levels
- Long-lasting immunosuppression (steroids, antibodies)
- Special attention should be considered in case of recent new symptoms such as:
  - Fever
  - Cough
  - Sore throat
  - Labored breathing
  - Muscle pain
  - Fatigue
  - Anosmia
  - Dysgeusia

Test to Confirm the Diagnosis (If they have not already done so)

Coronaviruses are positive single-stranded RNA viruses covered by a structure of glycoprotein's and lipids. That means that, unlike us humans, SARS-CoV-2 has its genetic material in the form of RNA. But ... PCR was only capable of amplifying DNA, right? True, DNA polymerases can only use DNA as template and not RNA. So how is it possible to use PCR to detect coronavirus infection? Well ... using a variant of standard PCR, RT-PCR, which uses the help of a very particular enzyme, reverse transcriptase?

The SAR-CoV-2 RT-PCR test should be proposed to all patients undergoing surgery, radiotherapy, chemotherapy or immunotherapy, if the ideal is feasible before each treatment/cycle, today impossible in our country!!! (Argentina)

Follow-up patients or cancer survivors should also be proposed if they have symptoms suggestive of COVID-19 infection. Serology should be proposed (if available) to identify previous COVID-19 infection in all cancer patients. If capacity is limited, the SARS-CoV-2 RT-PCR test should be proposed to all patients with symptoms suggestive of COVID-19 infection, in active treatment, in the follow-up phase, or in a survivor.

If serology is limited, it should be proposed to all patients undergoing surgery, radiotherapy, chemotherapy or immunotherapy, or any active anticancer treatment. Assess severity based on clinical, radiological, and pulmonary function.

Oncological Treatment Strategy Suggestions

Communication, discussion with other professionals and with patients is recommended, preferably by phone instead of face-to-face.

Decisions for initiation or continuation of treatment should be discussed for both uninfected patients and patients with SARS-CoV2 positive if they are symptomatic or mini-symptomatic, are still in a position to be treated and are willing to do so after an adequate

explanation of risk/benefit.

Discuss the benefits and risks of current cancer therapy in the context of the COVID-19 pandemic: Treatment setting, disease prognosis, patient comorbidities, patient preferences, likelihood, and risks of COVID-19 infection. If local treatment is planned for the early stage (surgery or radiation therapy), explore the possibilities of postponing the use of a "wait and see" approach (as in some prostate cancers) or prioritize treatment balancing the cost/benefit ratio. According to age, comorbidities and the impact on the result of the surgical procedure. If intravenous treatment is ongoing, you may temporarily switch to oral treatment, if available, to improve disease control.

Prioritize adjuvant therapies in patients with already-resected, high-risk relapse disease that is expected to yield significant absolute survival benefit.

Similarly, discuss the benefits and risks of palliative therapies and options for "stop and go" therapy vacations, maintenance, and switch to oral medications, if available, during the pandemic.

Consider other optional regimes and schedules to reduce visits to the hospital and/or Cancer Center or office. For patients under oral treatment, prefer telephone or web technology contacts for consultations and prescription renewal. If necessary, encourage phone or web technology contacts also for toxicity assessment, dose adaptation, and supportive care recommendation.

Discuss shorter/accelerated or hypo-fractionated radiation therapy schedules with radiation oncologists, where they are scientifically justified and appropriate for the patient.

Cancer Patients with Fever

- It should not be evaluated in day oncology centers.
- Initial evaluation outside the area with a high concentration of cancer patients or oncology personnel.
- The possibility of coronavirus should be consipraised and evaluated
- Stable patients should be treated with outpatient oral antibiotics.

The Oncologist

Reallocation of resources and restrictive security measures to face the pandemic can affect daily routines in the practice of oncology.

Some specific actions can help teams adapt their usual clinical practice to the new scenario. Improve teleconsultation services for stable patients, especially those receiving oral therapy, and re-evaluate regimen hours to reduce the number of clinic visits during the pandemic (three to two weeks instead of weekly, oral, or subcutaneous alternatives in intravenous administration site) should be encouraged. A "previous day" conference calling system should be recommended to identify flu-like symptoms in cancer patients so that appropriate action can be taken.

Protecting Yourself is Protecting Patients

Medical oncologists, as well as other healthcare workers, are currently exposed to risks that can put them at risk of COVID-19 infection, including exposure to pathogens, long work hours, and psychological distress.

Proper infection prevention and control training is key to ensuring that all medical personnel remain safe, thus ensuring safe cancer care settings for patients.

At work, the use of personal protective equipment is recommended. Strategies for dividing cancer healthcare personnel to rotate shifts that are epidemiologically consistent with the 14-day coronavirus incubation time can help ensure the safety and well-being of teams.

At home, medical oncologists are encouraged to follow basic protective measures against the new coronavirus as recommended by the WHO (for example, wash your hands frequently, practice social distancing).

Conclusion

Physicians caring for patients during the COVID-19 pandemic should assess the utility of any intervention, taking into account the risk of exposure to the virus, given the environment of healthcare interruptions and limited resources for health care.

The combat plan during battle should include patience, communication, diligence, and resolution. Risks must be valued very well, public health strategies must be thoroughly implemented, and resources must be used wisely. The elderly and patients with comorbidities, including cancer, are more vulnerable to COVID-19 infection; they may also be more at risk after receiving cancer treatment.

Some solid tumors and hematologic malignancies require immediate treatment, but others do not. The quality of the data in some cases is inadequate to support claims of a uniform approach applicable to every patient.

Experienced oncologists should be confident in exercising their judgment in deciding which patients need to start or continue treatment, due to the more aggressive biological characteristics of their tumor, versus those who can tolerate a postponement.

In the context of COVID-19 infection, the uselessness of treating people with advanced cancer disease should be frankly considered and discussed.

Patients receiving regular cancer treatment, including those recruited into clinical studies during the pandemic may disrupt social distancing and increase the likelihood of spreading the virus; therefore the supply of drugs used in clinical studies may also be interrupted.

The expanded use of telemedicine can help preserve social distancing and reduce the burden placed on the health care system. Although most cancer care is not usually considered 'elective', as resource constraints increase due to supply chain problems, variations in geographic needs, and the reallocation of medical infrastructure to care for infected patients, it will be necessary to make some modifications so that our patients receive the best available treatment and so that our doctors preserve their health.

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