



Den Cancer care during the spread of coronavirus disease 2019 (COVID-19) in Italy: young oncologists' perspective

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Received 24 March 2020 Accepted 24 March 2020 (CoV), named SARS-CoV-2 or 2019-nCoV, has been identified as the microbial agent causing viral pneumonia in several patients epidemiologically linked to a seafood market in Wuhan (Hubei province, China). ¹² Since then, the spread of coronavirus disease 2019

At the end of 2019, a novel severe acute

respiratory syndrome (SARS) coronavirus

(COVID-19) has progressively involved countries outside China leading the World Health Organization (WHO) to make the assessment that COVID-19 can be characterised as a pandemic.3

Outside China, Italy has the largest COVID-19 outbreak with 37 860 confirmed cases and 4032 deaths according to the data of 'Istituto Superiore di Sanità' on 20 March 2020. In order to limit viral spread, the Italian Government has implemented extraordinary measures which culminated on 9 March in a lockdown inhibiting—unless strictly required—people's movements and social activities throughout the national territory.

The Italian National Health System is currently under pressure and remarkable efforts are spent to provide an efficacious reaction to the emergency. As Italy is experiencing a chronic shortage of healthcare workers, the government announced a plan to recruit 20 000 new doctors, nurses and hospital employees, to meet public demand, on 9 March.⁶ Retired doctors may be called on as well as residents who have completed their medical degree and are in the final year of specialist training. Meanwhile, doctors who have come into contact with patients affected by COVID-19 are encouraged to work unless they show symptoms of the infection or have a positive test for SARS-CoV-2. However,

allowing untested healthcare personnel to take care of patients may be a double-edged sword due to the fact that undocumented infections may be the primary source of documented cases.⁷ Moreover, shortages of personal protective equipment (PPE) appear to be widespread across the health service and include general practitioner practices as well as hospitals.

Specific algorithms and protocols within the Emergency Medical System are being implemented, including the attempt to increase intensive care unit (ICU) capacity.^{8 9} For this purpose, especially in most affected areas, medical specialists including oncologists have been recruited to provide their assistance in managing patients suffering from COVID-19 requiring hospitalisation in ICUs, departments of infectious or respiratory diseases, or general internal medicine.

Older adults and patients with pre-existing comorbidities (commonly diabetes and cardiovascular disease) are facing the most severe and critical consequences of the SARS-CoV-2 outbreak. 10 11 Age is also a risk factor for cancer development, 12 and patients with cancer are more susceptible to infections as compared to healthy subjects due to systemic immunosuppression secondary to both the malignancy and anticancer treatments.¹³ Hence, the current emergency is of particular concern to medical oncologists and their patients. In the first article focusing on oncological cases affected by COVID-19, Liang and colleagues concluded that the risk of SARS-CoV-2 infection was higher in patients with cancer who deteriorated more rapidly in the clinic and had a higher risk of severe events including the necessity for

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admission to the ICU or death.¹⁴ Older age remained the only risk factor associated with severe events from SARS-CoV-2 infection among patients with cancer. The authors suggested three measures for reducing the burden of COVID-19 in oncology in endemic areas: to postpone treatments or elective surgery for stable cancer in endemic areas, to provide stronger personal protection provisions to patients and, finally, to offer more intensive surveillance or treatment for patients infected with SARS-CoV-2.¹⁴ In this situation of emergency for health-care systems, the inability to receive needed medical services is an additional concern.¹⁵

The issue on how to organise cancer care during the COVID-19 pandemic is crucial. ¹⁶ In order to provide some guidance on cancer care during the Italian SARS-CoV-2 outbreak, the Italian Association of Medical Oncology (AIOM) in partnership with the boards of Academic Oncologists (COMU) and of Oncology Unit Directors (CIPOMO) has recently proposed some critical recommendations for patients currently receiving active treatments, those in follow-up (ie, out of active treatment), as well as for the admission of patients and their caregivers to the hospital. ¹⁷

For patients currently receiving active treatments, oncologists are invited to consider, on a case-by-case basis, the possibility of a delay in treatment administration. The decision of confirming the scheduled administration or delaying treatment should be based on the biological features of the tumour, the clinical condition of the patient with his/her symptoms, treatment characteristics (ie,

expected benefit and adverse events including myelosup-pression), disease response to current anticancer therapy, and the potential risks for an infection with SARS-CoV-2. An alert about the use of checkpoint inhibitors is raised by the identification of the cytokine storm-induced hyper-inflammation as a pathogenetic mechanism for COVID-19-associated pneumonia of severe clinical scenarios. However, it should be recognised that an evidence-based estimation of the impact of treatment delay or interruption on the risk/benefit balance for each individual patient is currently lacking.

For patients who are currently in follow-up (ie, out of active treatment), oncologists should consider to avoid disease-free patients coming to the hospital for routine follow-up visits. A phone call/online exchange of clinical documentation can be useful to reassure patients, and refrain from consultation at the hospital except for the case of an emergence of new symptoms or new clinical or radiological signs of disease progression.

Regarding admission to the hospital, outpatients scheduled for treatment should come alone and avoid the assistance by a caregiver except for documented need of continuous assistance. Triage of patients with fever and/or respiratory symptoms is essential to prevent exposure to other patients and healthcare providers. ¹⁷

As young oncologists working in different regions, we are all implementing these recommendations (table 1). The overall goal of all these recommendations is the attempt to maintain cancer care in the frame of an environment as safe as possible for both patients and

Table 1 Practical suggestions on how to implement cancer care during the COVID-19 outbreak

Patients currently receiving or who need to start active treatments Patients in follow-up (currently out Admission of patients and to start active treatments of active treatment) Caregivers to the hospital

- Case-by-case evaluation of the risk/ benefit ratio of delaying anticancer treatment*
- Start or continue all adjuvant/ neoadjuvant treatments (or any other potentially curative therapy), as well as first-line therapies for metastatic disease
- Delay all treatments beyond first-line therapy with modest efficacy expected 2. (unless there are urgent clinical reasons), maintenance therapies and treatments in patients with low disease burden and slow progression 3.
- Delay imaging procedures to monitor treatment response (unless there are urgent clinical reasons)
- Shipment of oral drugs or dispensing of multiple treatment cycles, if feasible, based on supply availability and patients' characteristics
- Replace scheduled visits not associated with therapy prescription/ administration with email or phone contact (unless there are urgent clinical reasons)

- Phone call by the clinician in order to perform a quick triage of the clinical condition, and allow the examination of lab and/or imaging exams*
- To allow access to the hospital for regular consultations in the following cases:Suspected disease progression
- Need for a new prescription of active treatments (eg, adjuvant endocrine therapy for breast cancer)
- 3. Strong desire of the patients to perform a regular physical examination
- No caregiver allowed for all outpatients scheduled for treatment except in the case of documented need of a continuous assistance*
- Maximum one caregiver allowed (after triage) for every inpatient
- Quick triage of clinical condition before entering the hospital; no access allowed in the case of fever and/or respiratory symptoms (COVID-19 path to be followed in these cases)*
- Surgical masks and handwashing with hydrohalcoholic gel provided to all patients at the entrance
- Limiting points of entry to the hospital with separated paths for accessing the hospital for patients and hospital personnel

Other occasions of regular face-to-face interaction

- To avoid all face-to-face meetings (including multidisciplinary tumour boards that can be virtually organised), congresses, seminars and lectures intended for residents and PhD fellows, visits from pharmaceutical companies
- Cancellation of any group activity (eg, group therapy, recreational activities, etc)

^{*}Corresponding to the recommendations published by the Italian Association of Medical Oncology (AIOM) in partnership with the boards of Academic Oncologists (COMU) and of Oncology Unit Directors (CIPOMO).

COVID-19, coronavirus disease 2019.



healthcare providers. Notwithstanding some adaptations based on the specific directives of single institutions, the high level of homogeneity on how these measures are being implemented across centres is reassuring for the Italian oncology community and patients with cancer.

However, some opinions diverging from the described strategies have been voiced: for example, some colleagues have raised concerns regarding the delay of treatment for advanced disease or cancer screenings of healthy individuals. ¹⁹ We believe that in the context of the current emergency situation and considering the severely increased strain on our National Health System, the delay of the mentioned procedures is reasonable and realistically unavoidable. We are not advocating distraction, but we are clearly pointing to the necessity to save the life of thousands of people. As we are facing a rapidly evolving and unprecedented emergency, we are all forced to constantly reconsider and critically re-evaluate our opinions.

Special additional challenges for oncologists include the differential diagnosis between SARS-CoV-2 infection and clinical and radiological findings related to drugmediated toxicity (eg, immunotherapy), other infectious agents or cancer progression requiring specialised expertise of medical oncologists. Moreover, the management of patients with cancer also affected by COVID-19 represents a further need which should guarantee both active and potentially life-saving anticancer treatments as well as palliative and end-of life care.

In addition to the above recommendations, face-to-face interactions should be consistently restricted in this emergency period (table 1). As young oncologists living in the era of technology and social media, this difficult moment may serve as the basis to implement telemedicine whenever possible and feasible. Massive efforts should be put into monitoring of patients at home with regular contacts by telephone, electronic text transmission, email or smartphone apps. In these particular situations, such strategies could also help to alleviate patient isolation and loneliness by psychological interventions. Although 'telehealth' cannot be the only future strategy of medicine considering the relevance of patient-doctor interactions which are of special relevance in the field of oncology, the current crisis of the healthcare system necessitates the use of electronic communication as a valid tool to further optimise cancer care (eg, management of follow-up visits, oral therapies, etc) in such difficult circumstances.

As a final important note, the COVID-19 crisis is also hindering cancer research. Special considerations related to this regard should be highlighted and faced also considering the particular heterogeneity of available resources in the different units across the country (Box 1). The Food and Drug Administration, the European Medicines Agency (EMA) and the Italian Medicines Agency have issued special guidance for the conduction of clinical trials during the COVID-19 emergency. 21–23

Despite all these challenges associated with the COVID-19 epidemic in Italy, we as professionals who take care of a frequently frail patient population in a delicate

Box 1 Main challenges for cancer research during the COVID-19 outbreak

- Minimise or delay the opening of new clinical trials.
- Limit or hold patients' accrual in ongoing trials requiring extra procedures as compared with clinical practice.*
- Need to refer on-study patients to other active centres in the case of difficulties in continuing the planned treatment due to COVID-19related reorganisation.
- Smart working for data managers and study coordinators.
- Possible treatment delays or problems in drug supply for logistic reasons around COVID-19.
- Need for telephone contact report to replace in-person follow-up visits to be included within the patient's clinical notes.
- Cancel or delay onsite monitoring visits.
- Preserve both scientific validity of results and safety of patients and trial staff by implementing decision sharing and strict contacts with the sponsors.

*This decision should be based on multiple aspects: the structure and organisation of the oncology centre and the consequent ability to ensure extra procedures (ie, independent cancer centre or oncology department integrated within a general hospital), the type of study and the burden of extra procedures required, ethical considerations related to trial design (ie, presence of a placebo arm), the expected benefit that the patient could derive from the participation into the trial.

phase of their life should make all the possible efforts to mitigate the risk of suboptimal management of patients with cancer including those with concurrent COVID-19 infection. Considering the added extra burden of the epidemic for our patients and for all healthcare providers, also including the hard consequences of social distancing and isolation as well as a restriction in family interactions, the provision of encouragement and emotional help is essential. Our generation is facing such a tremendous crisis for the first time, but our commitment and extra energy as young oncologists are crucial to fight and succeed in this difficult situation which calls for the continuation of the provision of compassionate and safe care for our patients with cancer.

Our young oncologists' perspective (YOP) on protection against COVID-19 can be summarised by making the same acronym Y-O-P.

Protect:

- ➤ Yourself, and your family: at work, with constant focus and attention on PPE, and in personal life, by following all the official instructions and respecting lifestyle restrictions.
- ▶ Oncological care of our patients, delaying what can be delayed, but trying as much as possible to minimise the impact of the emergency on the usual standard of care.
- ▶ Patients' themselves from being infected, making any possible effort to minimise the risks and giving continuous direction and appropriate official information.

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REFERENCES

- Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382:727–33.
- 2 Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet* 2020;395:565–74.
- 3 World Health Organization. Available: https://www.who.int/dg/ speeches/detail/who-director-general-s-opening-remarks-at-themedia-briefing-on-covid-19-11-march-2020
- 4 Istituto Superiore di Sanità. Available: https://www.epicentro.iss.it/coronavirus/sars-cov-2-sorveglianza-dati
- 5 Remuzzi A, Remuzzi G. COVID-19 and Italy: what next? *Lancet* 2020. doi:10.1016/S0140-6736(20)30627-9. [Epub ahead of print: 13 Mar 2020].
- 6 Gazzetta Ufficiale della Repubblica Italiana, 2020. Available: https://www.gazzettaufficiale.it/eli/qu/2020/03/09/62/sq/pdf
- 7 Li R, Pei S, Chen B, et al. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2). Science 2020;6:eabb3221.
- 8 Spina S, Marrazzo F, Migliari M, et al. The response of Milan's emergency medical system to the COVID-19 outbreak in Italy. *Lancet* 2020;395:e49–50.
- 9 Grasselli G, Pesenti A, Cecconi M. Critical care utilization for the COVID-19 outbreak in Lombardy, Italy: early experience and forecast during an emergency response. *JAMA* 2020. doi:10.1001/ jama.2020.4031. [Epub ahead of print: 13 Mar 2020].
- Murthy S, Gomersall CD, Fowler RA. Care for critically ill patients with COVID-19. JAMA 2020. doi:10.1001/jama.2020.3633. [Epub ahead of print: 11 Mar 2020].
- 11 Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese center for disease control and prevention. *JAMA* 2020. [Epub ahead of print: 13 Mar 2020].
- 12 Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin 2020:70:7–30.
- 13 Kamboj M, Sepkowitz KA. Nosocomial infections in patients with cancer. *Lancet Oncol* 2009;10:589–97.
- 14 Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol 2020;21:335–7.
- 15 Xia Y, Jin R, Zhao J, et al. Risk of COVID-19 for cancer patients. Lancet Oncol 2020. doi:10.1016/S1470-2045(20)30150-9. [Epub ahead of print: 03 Mar 2020].
- 16 Ueda M, Martins R, Hendrie PC, et al. Managing cancer care during the COVID-19 pandemic: Agility and collaboration toward a common goal. J Natl Compr Cancer Netw 2020.
- 17 Rischio infettivo da Coronavirus COVID 19: indicazioni per l'Oncologia da parte del Presidente AIOM, del Presidente eletto AIOM, del Presidente CIPOMO e del Presidente COMU. Available: https://www.aiom.it/wp-content/uploads/2020/03/20200313_COVID-19_indicazioni_AIOM-CIPOMO-COMU.pdf
- 18 Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020. doi:10.1016/S0140-6736(20)30628-0. [Epub ahead of print: 16 Mar 2020].
- 19 Francesco C, Pettke A, Michele B, et al. Managing COVID-19 in the oncology clinic and avoiding the distraction effect. Ann Oncol 2020. doi:10.1016/j.annonc.2020.03.286. [Epub ahead of print: 19 Mar 2020].
- 20 Hollander JE, Carr BG. Virtually perfect? telemedicine for Covid-19. N Engl J Med 2020. doi:10.1056/NEJMp2003539. [Epub ahead of print: 11 Mar 2020].
- 21 Food and Drug Administration (FDA). Available: https://www.fda.gov/media/136238/download
- 22 . European Medicines Agency (EMA). Available: https://www.ema.europa.eu/en/news/guidance-sponsors-how-manage-clinical-trials-during-covid-19-pandemic
- 23 Agenzia Italiana del Farmaco (AIFA). Available: https://www.aifa.gov. it/documents/20142/871583/Comunicato_gestione_studi_clinici_in_emergenza_COVID-19_EN_12.03.2020.pdf/ee1f33e3-bb3e-9ce9-2a93-b33e88eea94d

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