Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Clinical Oncology 33 (2021) e50–e53

Contents lists available at ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Editorial

Coronavirus Disease 2019: the Pivotal Role of UK Clinical Oncology and the UK Coronavirus Cancer Monitoring Project

J. Best [*], T. Starkey [†], A. Chatterjee [*], D. Fackrell [‡], L. Pettit [*], N. Srihari [*], H. Tween [§], A. Olsson-Brown [¶], V. Cheng [‖], D.J. Hughes [**], A.J.X. Lee [††], K. Purshouse [‡‡], R. Arnold [†], UK Coronavirus Cancer Monitoring Project Team [†¶¶], S. Sivakumar [§§], J.-B. Cazier [†¶¶], L.Y.W. Lee [†]

[*] *Shrewsbury and Telford Hospital NHS Trust, Royal Shrewsbury Hospital, Shrewsbury, UK*
[†] *Institute of Cancer and Genomic Sciences, University of Birmingham, Birmingham, UK*
[‡] *Queen Elizabeth Hospital, University Hospitals Birmingham, Birmingham, UK*
[§] *University Hospitals Coventry and Warwickshire, Coventry, UK*
[¶] *The Clatterbridge Cancer Centre, Birkenhead, Wirral, UK*
[‖] *Leeds Cancer Centre, Bexley Wing, St James's University Hospital, Leeds, UK*
[**] *Department of Cancer Imaging, Division of Cancer Studies, Guy's Campus, King's College London, London, UK*
[††] *University College London, UCL Cancer Institute, London, UK*
[‡‡] *Edinburgh Cancer Centre, Western General Hospital, Edinburgh, UK*
[§§] *Department of Oncology, University of Oxford, Oxford, UK*
[¶¶] *Centre for Computational Biology, University of Birmingham, Birmingham, UK*

Received 15 April 2020; received in revised form 20 May 2020; accepted 28 May 2020

The UK is currently in the middle of the coronavirus disease 2019 (COVID-19) pandemic. The causative virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a novel strain of coronavirus previously unidentified in humans and thought to be of zoonotic origin [1]. SARS-CoV-2 exposure may result in a wide variety of outcomes, ranging from asymptomatic infection to the development of respiratory failure requiring ventilatory support [2]. COVID-19 is extremely contagious and as of 20 May 2020, there were over 250 000 cases and 35 000 deaths reported in the UK alone [3,4].

Globally there has been huge disruption to everyday life. Without a vaccine or effective treatment, governments are reliant upon strategies such as social distancing and quarantine measures to limit SARS-CoV-2 infection to a level that can be managed by healthcare systems [5]. Furthermore, the additional burden placed on healthcare services will probably affect the quality of care for patients suffering with unrelated health problems. This is of particular relevance to oncologists, as prompt diagnosis and treatment can make significant difference to patient outcomes. In addition, individuals with a significant comorbidity such as cancer may be particularly vulnerable to coronavirus infection as a potential consequence of their immunosuppressed state [6–8].

This leaves us as oncologists faced with challenging decisions about how to proceed with treatment for patients with cancer. The risks of COVID-19 infection have to be incorporated into our decision making and will impact on our practice for months or potentially years to come. This has led to the need to have difficult conversations with patients about how the COVID-19 pandemic affects their treatment, with realistic weighing up of the potential benefits and harms that can occur. In our experience, most patients have been remarkably pragmatic about the current situation and the measures we are putting in place, but this is an emotive area and conversations about stopping or delaying treatment are difficult. To effectively and compassionately have these conversations we need to be informed by the best evidence available and at present this is limited. Much of the current published literature around COVID-19 and cancer are guidelines and the published studies we have are largely based around smaller numbers of patients in the Chinese population.

The Liang *et al.* [7] study included 18 patients with a confirmed diagnosis of both COVID-19 and cancer out of a

Author for correspondence: L.Y.W. Lee, Institute of Cancer and Genomic Sciences, University of Birmingham, Edgbaston, Birmingham B15 2TT, UK. Tel: +44-121-414-3511.
E-mail address: L.lee.2@bham.ac.uk (L.Y.W. Lee).

https://doi.org/10.1016/j.clon.2020.05.021

total of 2007 cases. This study noted worse outcomes in the cancer cohort, with seven (39%) suffering a severe adverse outcome compared with 124 (8%) overall [7]. The report by Zhang *et al.* [9] showed similar outcomes, with 15 (53.6%) of 28 included patients suffering severe events with a 28.6% mortality rate (eight deaths). Yu *et al.* [8] identified 12 cancer patients from their population of 1524, three of whom died.

The largest currently reported cohort of patients compared 105 patients with both COVID-19 and cancer with 536 matched non-cancer patients [10], reporting a higher rate of both mortality (odds ratio 2.34) and intensive care unit admission (odds ratio 2.84) in patients with cancer compared with the control group. In particular, higher rates of mortality (odds ratio 5.58) and intensive care unit admission (odds ratio 6.59) were observed in stage IV cancer patients; non-metastatic cancer patients had similar outcomes to the matched control group. Cancer patients also had a longer mean length of stay at 27 days compared with 17.75 days in the control group.

Patients with lung cancer were the largest cohort represented in these studies. Dai *et al.* [10] reported that lung cancer represented 20.95%, followed by gastrointestinal 12.38% and breast 10.48%, with haematological cancer representing 8.57% of cases [10]. Although a smaller proportion of total cases, the highest mortality rate was noted in patients with haematological cancers (33.3% of nine patients); lung cancer patients had a mortality rate of 18.8% (four of 22 cases).

With the limitations on hospital resources meaning the usual support to manage anticancer treatment toxicities are potentially reduced or unavailable and with the additional risk to patients with cancer who contract a concurrent COVID-19 infection [7,8], oncological treatments that may confer an unacceptable risk as perceived by patients and clinicians are being altered, cancelled or deferred. Guidance has been produced as to how to best balance the risks of treating against the risks of changing away from the standard treatment, such as the Royal College of Radiologists' guidelines for radiotherapy during the COVID-19 pandemic [11–16].

Pragmatically, in the absence of a definite understanding of how COVID-19 will affect patients with cancer, the key approach has been to minimise the chance of the patient contracting COVID-19 infection. A number of strategies have already been adopted by the majority of UK cancer centres to mitigate this risk, including delivery of outpatient reviews by telephone rather than in the clinic, deferral of non-urgent anticancer treatments and shortening of radiotherapy fractionation schedules. The available evidence of efficacy [17–22] has been balanced against what we know of the risks from COVID-19 to form consensus guidance.

The available studies note that recent treatment affected outcomes, but this impact differed between modalities and small patient numbers limit the ability to draw conclusions. Liang *et al.* [7] reported severe adverse events in three of four patients treated within the previous month; Zhang *et al.* [9] noted more frequent adverse events in those treated within 14 days (hazard ratio 4, $n = 6$) and Dai *et al.* [10] reported that patients receiving radiotherapy (12.26%) within 40 days prior to infection did not show worse outcomes compared with the age-matched controls, but the six patients (5.7%) receiving immunotherapy had a 33% mortality rate. This poor outcome was hypothesised to relate to an acute respiratory distress syndrome induced by a cytokine storm and contrasts with Bersanelli's [23] hypothesis that immunotherapy could be protective against COVID-19, although noting the possibility that immune toxicity such as pneumonitis and COVID-19 infection coinciding could cause worse outcomes and that both COVID-19 and anti-PDL1 agents can cause a cytokine release syndrome leading to acute respiratory distress syndrome.

Despite the uncertainty about which treatments are safe to continue and the full extent of the risks from the COVID-19 pandemic, the risk to patients from the underlying malignancy should not be ignored. Although considering nine paediatric patients, Hrusak *et al.* [24] noted that the risks of harm from untreated malignancy appeared to outweigh the risks from COVID-19 in the paediatric population. Although potentially children are less impacted by COVID-19 compared with adults, this would emphasise the importance of continuing to treat patients where safe to do so. As more evidence of the true impact of COVID-19 on the UK population becomes available, we will need to continue to review the guidelines to make the best use of the evidence available to support safe practice and enable an informed discussion with patients about the risks of treatment [25–28]. Despite the increased difficulty of treating cancer patients at present, medical professionals from around the UK have shown themselves to be adaptable and resilient. This collaborative, cross-disciplinary approach has been hugely important in optimising the delivery of patient care, enabled by our ability to share information about our experiences. A core part of this going forward will be the UK Coronavirus Cancer Monitoring Project, which aims to monitor the impact of COVID-19 on cancer patients and enable oncologists to gain crucial insights and inform clinical- and infrastructure-based decision making.

The UK Coronavirus Cancer Monitoring Project was launched on 18 March 2020 following discussions between clinical oncologists in our cancer centres. The project consists of a Local Emergency Response Reporting Group at each of our cancer centres and enables data collection on SARS-CoV-2-positive cancer patients. The primary end point measure of this study will be all-cause mortality following a hospitalisation for a laboratory confirmed SARS-CoV-2 infection. The project will attempt to define factors that are associated with increased mortality/morbidity from COVID-19, including patient factors (age, gender, comorbidities, smoking status, and ethnicity), cancer factors (subtype, stage), cancer treatment (intent, modality, line of treatment) and COVID-19 symptoms and treatments.

To date, there are over a 1300 patients in the registry. Potentially of interest to the readership is that there are >100 patients who have had radiotherapy within 4 weeks of admission. This subgroup is increasing in size and will hopefully enable the clinical oncology community to

answer some of the aforementioned clinical questions given enough time and collaboration. Therefore, we believe this pan-UK information is key to understanding the interactions between COVID-19 and our treatment regimens.

The project will continue to analyse and disseminate data in real time. This will enable our cancer centres to assess the impact coronavirus is having on cancer patients, assess the impact of our treatment interventions and potentially allow the maintenance of the best possible standard of cancer patient care within challenging circumstances.

For more information about the UK Coronavirus Cancer Monitoring Project, see https://ukcoronaviruscancermonitoring.com.

Conflicts of Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: T. Starkey, A. Olsson-Brown, V. Cheng, D.J. Hughes, A.J.X. Lee, K. Purshouse, R. Arnold, C. Palles, S. Sivakumar, J.-B. Cazier and L.Y.W. Lee comprise part of the UK Coronavirus Monitoring Project team, donating time and resources to support the project. No other conflicts of interest are declared.

References

[1] Lake MA. What we know so far: COVID-19 current clinical knowledge and research. *Clin Med* 2020;20(2):124–127.

[2] Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, *et al*. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med* 2020. https://doi.org/10.1016/S2213-2600(20)30079-5.

[3] Coronavirus COVID-19 (2019-nCoV). Available at: https://www.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6.

[4] Coronavirus disease 2019 (COVID-19) Situation Report-72 highlights. Available at: www.who.int/epi-win.

[5] Walker P, Whittaker C, Watson O, Baguelin M, Ainslie KEC, Bhatia S, *et al. The global impact of COVID-19 and strategies for mitigation and suppression.* 2020. Available at: https://www.imperial.ac.uk/media/imperialcollege/medicine/sph/ide/gida-fellowships.Imperial-College-COVID19-Global-Impact-26-03-2020v2.pdf.

[6] Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, *et al*. Clinical characteristics of 2019 novel coronavirus infection in China. *N Engl J Med* 2020;382:1708–1720. https://doi.org/10.1056/NEJMoa2002032.

[7] Liang W, Guan W, Chen R, Wang W, Li J, Xu K, *et al*. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol* 2020;21:335–337.

[8] Yu J, Ouyang W, Chua MLK, Xie C. SARS-CoV-2 transmission in patients with cancer at a tertiary care hospital in Wuhan, China. *JAMA Oncol* 2020. https://doi.org/10.1001/jamaoncol.2020.0980.

[9] Zhang L, Zhu F, Xie L, Wang C, Wang J, Chen R, *et al*. Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. *Ann Oncol* 2020. https://doi.org/10.1016/j.annonc.2020.03.296.

[10] Dai M, Liu D, Liu M, Zhou F, Li G, Chen Z, *et al*. Patients with cancer appear more vulnerable to SARS-COV-2: a multi-center study during the COVID-19 outbreak. *Cancer Discov* 2020. https://doi.org/10.1158/2159-8290.CD-20-0422.

[11] Royal College of Radiologists. *The timely delivery of radical radiotherapy: guidelines for the management of unscheduled treatment interruptions*, 4th ed. 2019. Available at: www.rcr.ac.uk.

[12] Jones B, Dale RG, Hopewell J. Additional guidance on management of unscheduled radiotherapy treatment interruptions in patients during the COVID-19 pandemic. Available at: www.rcr.ac.uk/cancer-treatment-documents.

[13] Patel K, Choudhury A, Hoskin P, Varughese M, James N, Huddart R, *et al*. Clinical guidance for the management of patients with urothelial cancers during the COVID-19 pandemic – rapid review. *Clin Oncol* 2020. https://doi.org/10.1016/j.clon.2020.04.005.

[14] O'Cathail SM, Gilbert DC, Sebag-Montefiore D, Muirhead R. Challenges and consequences of COVID-19 in the management of anorectal cancer: coming together through social distancing. *Clin Oncol* 2020. https://doi.org/10.1016/j.clon.2020.04.009.

[15] Faivre-Finn C, Fenwick J, Franks K, Harrow S, Hatton M, Hiley C, *et al*. Reduced fractionation in lung cancer patients treated with curative-intent radiotherapy during the COVID-19 pandemic. *Clin Oncol* 2020. https://doi.org/10.1016/j.clon.2020.05.001.

[16] Jones CM, Hawkins M, Mukherjee S, Radhakrishna G, Crosby T. Considerations for the treatment of oesophageal cancer with radiotherapy during the COVID-19 pandemic. *Clin Oncol* 2020. https://doi.org/10.1016/j.clon.2020.04.001.

[17] Brunt AM, Haviland J, Sydenham M, Al-hasso A, Bloomfield D, Chan C, *et al*. OC-0595: FAST-Forward phase 3 RCT of 1-week hypofractionated breast radiotherapy: 3-year normal tissue effects. *Radiother Oncol* 2018;127:S311–S312.

[18] Brunt AM, Haviland J, Sydenham M, Algurafi H, Alhasso A, Bliss P, *et al*. FAST phase III RCT of radiotherapy hypofractionation for treatment of early breast cancer: 10-year results (CRUKE/04/015). *Int J Radiat Oncol* 2018;102(5):1603–1604.

[19] Chan AK, Sanghera P, Choo BA, McConkey C, Mehanna H, Parmar S, *et al*. Hypofractionated accelerated radiotherapy with concurrent carboplatin for locally advanced squamous cell carcinoma of the head and neck. *Clin Oncol* 2011;23(1):34–39.

[20] Fong CTK, McConkey C, Sanghera P, Hartley A, Rahman JK, Nutting C, *et al*. OC-0274: Effect of radiotherapy technique/fractionation on 2-year primary local control in the PET-NECK study. *Radiother Oncol* 2018;127:S139.

[21] Nutting CM, Morden JP, Harrington KJ, Urbano TG, Bhide SA, Clark C, *et al*. Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial. *Lancet Oncol* 2011;12(2):127–136.

[22] Benghiat H, Sanghera P, Cashmore J, Hodson J, Mehanna H, Simmons R, *et al*. Four week hypofractionated accelerated intensity modulated radiotherapy and synchronous carboplatin or cetuximab in biologically staged oropharyngeal carcinoma. *Cancer Clin Oncol* 2014;3(2):1.

[23] Bersanelli M. Controversies about COVID-19 and anticancer treatment with immune checkpoint inhibitors. *Immunotherapy* 2020;12(5):269–273. https://doi.org/10.2217/imt-2020-0067.

[24] Hrusak O, Kalina T, Wolf J, Balduzzi A, Provenzi M, Rizzari C, *et al*. Flash survey on severe acute respiratory syndrome

coronavirus-2 infections in paediatric patients on anticancer treatment. *Eur J Cancer* 2020;132:11–16.

[25] Simcock R, Thomas TV, Mercy CE, Filippi AR, Katz MA, Pereira IJ, *et al*. COVID-19: global radiation oncology's targeted response for pandemic preparedness. *Clin Transl Radiat Oncol* 2020;22:55–68. https://doi.org/10.1016/j.ctro.2020.03.009.

[26] Coles CE, Aristei YC, Bliss J, Boersma L, Brunt AM, Chatterjee S, *et al*. International guidelines on radiation therapy for breast cancer during the COVID-19 pandemic. *Clin Oncol* 2020;32:279–281. Available at: https://doi.org/10.1016/j.clon.2020.03.006.

[27] Royal College of Radiologists. Head and neck cancer and COVID-19. Available at: www.rcr.ac.uk/cancer-treatment-documents.

[28] Royal College of Radiologists. Synopsis of ILROG recommendations for administering radiotherapy for hematological malignancies during emergency conditions of the COVID-19 pandemic. Available at: https://www.rcr.ac.uk/sites/default/files/ilrog-emergency-guidelines-covid19.pdf.