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Letter to the Editor

Prolonged SARS-CoV-2 viral shedding in patients with solid tumours and associated factors

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To the editor:

SARS-CoV-2 is a highly contagious virus and can cause potentially fatal complications in cancer patients [1–4]. Until now, the most accurate and common methods to detect active viral infection are: (1) a positive RT-PCR, (2) a serological test (IgM+ and IgG-), (3) or a positive antigen test [5]. Previous studies have characterised the time length of viral shedding in immunocompetent patients [6]; however, there are scarce reports on immunosuppressed cancer patients. Aydillo *et al.* studied shedding of viable SARS-CoV-2 in transplanted hematological patients or those receiving CAR-T cell therapy [7]. In fact, the CDC's recommendations for this patient profile are still based on limited data [8]. Thus, we aim to study SARS-CoV-2 viral shedding in patients with solid tumours and its associated factors.

For this study, we recruited all patients in our centre (Hospital Universitario Infanta Leonor, Madrid, Spain) diagnosed with solid tumours and COVID-19 from 1st March 2020 to 30th November 2020. COVID-19 diagnosis was based on positive nasopharyngeal RT-PCR. We prospectively followed the patients until SARS-CoV-2 shedding, defined as RT-PCR negativisation or incidence of positive IgG antibodies by ELISA. We made a descriptive analysis of our sample and then analysed the time until viral shedding. After this, we used Kaplan–Meier visualisation and cox regression models to study associated factors. The study was approved by the ethics committee of our centre (Code: COVID-CANCER-HUIL 213/20).

Of the 149 patients with solid tumours diagnosed with COVID-19 in our centre, 48 patients were finally selected and prospectively followed up (32.3%). Fifty-eight patients were excluded because they died during follow-up (38.9%). Another 43 patients were excluded because they were not able to be prospectively followed-up (28.8%).

In our study, 28 patients were male (58.3%), and the median age was 69 years. Twenty-nine patients received chemotherapy (60.4%), one immunotherapy (2.1%) and 18 patients other treatments as targeted therapy or radiotherapy, among others (37.5%). The most predominant histology was lung cancer and breast cancer (n = 14, 29.2%; n = 10, 20.8%, respectively). Seven patients (14.6%) had localised disease, compared to 41 patients (85.4%) with locally advanced or metastatic disease. Only 3 patients received convalescent plasma

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Table 1
Clinical and demographical characteristics of the patients.

Characteristics	PCR <25 (n = 25)	PCR >25 (n = 23)	*p* value
Age (median)	68	71	0.7
Sex			
Female, n (%)	11 (44.0%)	9 (39.1%)	
Male, n (%)	14 (56.0%)	14 (60.8%)	0.7
Tumour localisation (more frequent)			
Lung, n (%)	8 (32.0%)	6 (26.1%)	0.7
Staging			
Localised, n (%)	6 (24.0%)	1 (4.4%)	
Advanced[a], n (%)	19 (76.0%)	22 (95.6%)	0.05
Oncological treatment			
Chemotherapy, n(%)	14 (56.0%)	15 (65.3%)	
Immunotherapy,n(%)	1 (4.0%)	0 (0%)	
Others, n(%)	10 (40.0%)	8 (34.7%)	0.5
COVID-19 treatment			
Convalescent plasma, n(%)	1 (4.0%)	2 (8.7%)	
Others[b], n(%)	11(44.0%)	13 (56.5%)	
No treatment, n(%)	13 (52.0%)	8 (34.8%)	0.4

[a] Advanced: defined advanced as locally advanced plus metastatic disease.
[b] Others COVID-19 treatment: dexamethasone, remdesivir, hydroxychloroquine, lopinavir/ritonavir.

transfusion (6.3%) and 24 specific treatment for COVID-19 (50.0%) (dexamethasone, hydroxychloroquine, lopinavir/ritonavir or remdesivir). Only one patient was admitted to the Intensive Care Unit (ICU) due to the severity of COVID-19. The median time until viral shedding was 22 days. We detected reactivations in 7 patients (14.6%) with positive RT-PCR and compatible symptoms; four were receiving the first cycle of chemotherapy after recovery from COVID-19.

Patients diagnosed with metastatic or locally advanced tumours mostly present positive RT-PCR for 25 days or more, compared to those with localised tumours (22/41−53.6%- versus 1/7 patients −14.2% -, $p = 0.05$). No differences between age (71 years old in patients with PCR≥25 versus 68 years old in patients with PCR>25; $p = 0.7$), sex ($p = 0.7$), tumour localisation ($p = 0.7$), cancer treatment class ($p = 0.5$), type of COVID-19 treatment ($p = 0.4$) or administration of COVID-19 hyperimmune plasma ($p = 0.4$) were

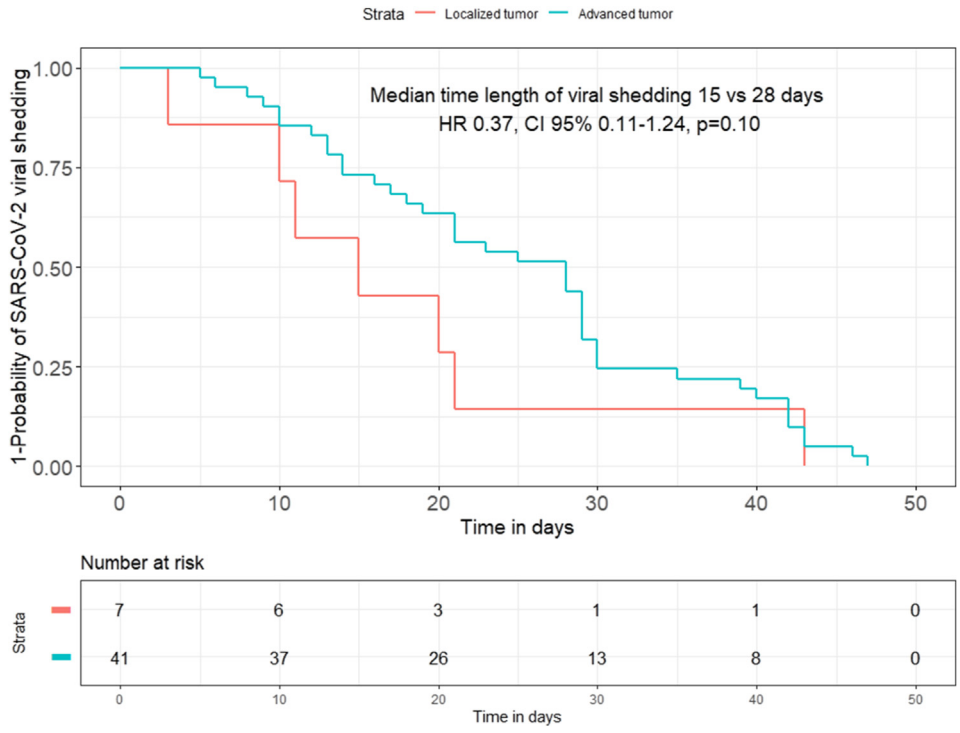

Fig. 1. Kaplan-Meier viral shedding comparing patients with localised tumours versus patients with advanced tumours.

detected (Table 1). Time to viral shedding was higher in those with advanced tumours (Fig. 1), although a trend towards statistical significance only was detected (28 days versus 15 days, $p = 0.10$); patients with localised tumours were less likely to present longer duration of COVID-19 until viral shedding (HR 0.37, CI 95% 0.11–1.24, $p = 0.10$). We found no further associations in terms of the types of tumour or COVID-19 treatments received, neither in terms of sex or age.

Regarding reactivations of COVID-19, we observed that lung cancer patients have a higher percentage of reactivations compared to breast cancer patients (4/14–28.4% - versus 1/10 -10% -, $p = 0.05$).

This is, to our knowledge, the first published cohort of patients with solid tumours studying viral shedding and its associated risk factors, although we are aware of the small sample size and that we developed a single-centre study. In our study, we observed that patients with advanced cancer at COVID-19 diagnosis have a greater risk of continuing to present positive RT-PCR with prolonged COVID-19 symptoms, similar to that observed in hematological patients undergoing transplant or CAR-T cell therapy [7]. In addition, we observed that these patients with advanced disease have the worst prognosis [1,2], like lung cancer patients and hematologic cancer patients [2,8]. The advanced state of immunosuppression induced by their cancer and by the specific oncological treatments received could justify our findings.

For this reason, as is suggested in two studies [7,10], we consider it a priority to review the current management recommendations in oncological patients to define when it is safe to finish isolation, as well as to restart treatment. Also, there is a need for further research in reactivations, especially in advanced cancer patients, hematologic and lung cancer patients, as they have had the worst prognosis in published series [1,2,9].

Authors contributions

J.R. contributed to the conception and design of the study, data acquisition, statistical analysis, interpretation of the data and writing of the manuscript. P.G. contributed to the statistical analysis, interpretation of the data and writing of the manuscript. B.O., G.S.M., A.M.M., M.P.*P. and* M.A.L. contributed to the conception and design of the study and interpretation of the data. All authors reviewed and approved the final version of the manuscript.

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Conflict of interest statement

The authors declare no conflict of interest for the present work.

References

[1] Rogado J, Obispo B, Pangua C, et al. Covid-19 transmission, outcome and associated risk factors in cancer patients at the first month of the pandemic in a Spanish hospital in Madrid. Clin Transl Oncol 2020 Dec;22(12):2364–8.
[2] de Joode K, Dumoulin DW, Tol J, Westgeest HM, et al., DOCC Investigators. Dutch Oncology COVID-19 consortium: outcome of COVID-19 in patients with cancer in a nationwide cohort study. Eur J Canc 2020 Dec;141:171–84.
[3] 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 Jul 1;6(7):1108–10.
[4] Elkrief A, Desilets A, Papneja N, et al. High mortality among hospital-acquired COVID-19 infection in patients with cancer: a multicentre observational cohort study. Eur J Canc 2020 Nov; 139:181–7. https://doi.org/10.1016/j.ejca.2020.08.017.
[5] Arons MM, Hatfield KM, Reddy SC, et al. Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility. N Engl J Med 2020;382:2081–90.
[6] Yan D, Liu XY, Zhu YN, et al. Factors associated with prolonged viral shedding and impact of lopinavir/ritonavir treatment in hospitalised non-critically ill patients with SARS-CoV-2 infection. Eur Respir J 2020 Jul 16;56(1):2000799.
[7] Aydillo T, Gonzalez-Reiche AS, Aslam S, van de Guchte A, et al. Shedding of viable SARS-CoV-2 after immunosuppressive therapy for cancer. N Engl J Med 2020 Dec 1. https://doi.org/10.1056/NEJMc2031670. NEJMc2031670.
[8] Centers for Disease Control and Prevention. Discontinuation of transmission-based precautions and disposition of patients with COVID-19 in healthcare settings (interim guidance). August 10, 2020. https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-hospitalized-patients.html.
[9] Rogado J, Pangua C, Serrano-Montero G, Obispo B, Marino AM, Pérez-Pérez M, et al. Covid-19 and lung cancer: a greater fatality rate? Lung Canc 2020 Aug;146:19–22.
[10] Reidy-Lagunes D, Saltz L, Postow M, et al. Recommendations for testing and treating outpatient cancer patients in the era of COVID-19. J Natl Cancer Inst 2020 Aug;14:djaa111. https://doi.org/10.1093/jnci/djaa111.