2 Whitley RJ. Herpes simplex virus infection. *Semin Pediatr Infect Dis* 2002; **13**: 6–11.
3 Chauvin PJ, Ajar AH. Acute herpetic gingivostomatitis in adults: a review of 13 cases, including diagnosis and management. *J Can Dent Assoc* 2002; **68**: 247–51.
4 Nasser M, Fedorowicz Z, Khoshnevisan MH, Shahiri Tabarestani M. Acyclovir for treating primary herpetic gingivostomatitis. *Cochrane Database Syst Rev* 2008; (4): CD006700.

Immune checkpoint inhibition in the era of COVID-19

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The worldwide coronavirus pandemic continues to result in significant morbidity and mortality, with almost 24 million confirmed cases to date. Approximately 80% of patients have mild disease and do not require hospitalization.[1] A key challenge facing the medical community is predicting which patients are at risk of developing severe disease, in order to initiate early supportive treatment and to facilitate enrolment into much needed prospective clinical trials, both crucial for developing and optimizing effective treatment strategies.

Patients with cancer have already been identified as having an increased risk of developing not only COVID-19 infection, but also severe disease, both of which are associated with poorer clinical outcomes.[2] Reassuringly, the increase in mortality from COVID-19 infection in patients with cancer may be primarily related to age, sex and comorbidities rather than to the cancer itself. Furthermore, there was no increased mortality in patients receiving and those not receiving anticancer therapy.[3]

Nevertheless, it is at least conceivable that the type of anticancer therapy may influence the risk and course of COVID-19 infection in patients with cancer. Given the increasing use of immune checkpoint inhibition in Dermatology (metastatic melanoma, Merkel cell carcinoma and squamous cell carcinoma) we reviewed the current literature to determine the extent to which immune checkpoint inhibition has been associated with COVID-19 infection.

We performed PubMed searches to 22 June 2020 using the search terms 'COVID-19' or 'SARS-CoV-2', and 'immune checkpoint', 'nivolumab', 'ipilimumab', 'pembrolizumab', 'avelumab', 'cemiplimab' or 'atezolizumab'. Only articles in English were included for further analysis.

We identified seven case reports and one case series of patients treated with immune checkpoint inhibitors who developed SARS-CoV-2 infections (Table 1), a total of 10 patients. An additional case of coronavirus HKU1 was reported.

Of the 10 patients with SARS-CoV-2, 30% were women and age range was 22–75 years. Half (50%) of the cases had an underlying urological tumour, 20% had metastatic melanoma, 20% had lung cancer and 10% had a haematological malignancy. Regarding treatment, 30% of the patients had received an anti-PD-L1 treatment (atezolizumab), 20% a combined anti-CTLA-4/anti-PD-1 treatment, 40% were treated with nivolumab (anti-PD-1) monotherapy and one patient (10%) received pembrolizumab (also anti-PD1). The effect of comorbidity, smoking status and ethnicity was difficult to ascertain as these were inconsistently recorded. Time from initiation of immune checkpoint inhibitor to the development of COVID-19 symptoms ranged from 48 h to > 1 year. The treatments for COVID-19 infection varied considerably, but 70% of cases received antibiotics, 20% antiviral medication and 30% received hydroxychloroquine (some patients received > 1 treatment). Three patients did not require specific therapy. The patient with coronavirus HKU1 received systemic corticosteroids for presumed checkpoint-mediated pneumonitis. In fact, the clinical and radiological presentation of immune checkpoint-related pneumonitis may be indistinguishable from that of SARS-CoV-2, making early SARS-CoV-2 PCR testing crucial. Three patients (30%) died due to coronavirus infection. Of the remaining patients, immune checkpoint therapy was recommenced or planned for four.

We found that only 10 patients with COVID-19 infection during immune checkpoint inhibition therapy have been reported. However, it is worth noting that 30% of the cases had a very mild clinical course and did not require hospitalization. Moreover, immune checkpoint therapy was safely recommenced in several patients. These points are extremely important given the fear and anxieties of patients with cancer regarding COVID-19 infection, which may lead some patients to unnecessarily delay or interrupt therapy.

Ultimately, the decision on whether to initiate and/or continue immune checkpoint therapy during the coronavirus pandemic must be based on a detailed consideration of several factors, including tumour burden and progression, comorbidities, existing immunosuppression, palliative vs. adjuvant treatment and alternative treatment options, and cannot be generalized.[4] Geographical coronavirus prevalence should also be considered. Irrespective of the final cancer treatment decision, the importance of facial coverings, social distancing, shielding and hand hygiene should also be emphasized.

Moving forward, there seems to be a strong case for a comprehensive and standardized prospective register of COVID infections during immune checkpoint inhibition therapy, at least at the local and national levels. This would provide vital information to determine how checkpoint inhibition influences the course of the disease,

Table 1 Details of the patients on immune checkpoint inhibitors with COVID-19 infection found in the literature.

Author	Serzan *et al.*, 2020[1]	Lovly *et al.*, 2020[2]	Szabados *et al.*, 2020[3]				Schmidle *et al.* 2020[4]	Artigas *et al.*, 2020[5]	Bonomi *et al.*, 2020[6]	Yekedüz *et al.*, 2020[7]	O'Kelly *et al.*, 2020[8]
Age, years	65	56	52	68	66	72	47	51	65	75	22
Sex	Male	Male	Male	Male	Male	Male	Female	Male	Male	Female	Female
Ethnicity	Caucasian	NS	NS	NS	NS	NS	NS	NS	NS	NS	Not stated
Comorbidities		Diabetes, COPD	Hypertension	Hypertension	Hypertension	Hypertension, diabetes	NS	NS	COPD	COPD, IHD/AF, hypertension, diabetes	Previous chemotherapy, brentuximab
Smoker	NS	Yes	No	Yes	No	Yes	NS	NS	NS	NS	NS
Cancer type	Stage IV melanoma	Small cell lung cancer	Renal cell carcinoma	Renal cell carcinoma	Urothelial carcinoma	Urothelial carcinoma	Stage IV melanoma adj.	Renal cell carcinoma	Lung adenocarcinoma	Stage IV melanoma	Hodgkin lymphoma
I-C treatment	Ipilimumab 3 mg/kg, nivolumab 1 mg/kg	Carboplatin, etoposide, atezolizumab	Ipilimumab, nivolumab	Ipilimumab, nivolumab	Atezolizumab	Atezolizumab	Nivolumab	Nivolumab	Nivolumab	Nivolumab	Pembrolizumab
Time to symptoms	48 h	48 h	2 cycles	1 cycle	6 months	4 months	7 months	4 months	7 months	27 cycles	6 cycles (every 6 weeks)
Symptoms	Dyspnoea; yellow sputum	Dyspnoea; chest pain cough	Steroids for irAE (rash) after 32 days; dyspnoea; fever; cough	Fever; cough	Dyspnoea. cough; pneumonitis treated with steroids	Cough; diarrhoea; renal failure	Cough; headache; fever; sore throat	Fatigue	Confusion; fever; dyspnoea	Diarrhoea; dyspnoea; fever	Cough; fever; sore throat
CT findings	Ground-glass infiltrates	Bilateral milk glass infiltrates	Bilateral lung infiltrates	NS	Fibrotic lung changes	NS	Unremarkable	Ground-glass opacities	CXR: interstitial changes	Bilateral pleural thickening	Bilateral infiltrates
SARS-Cov-2 PCR positive	Coronavirus HKU1-positive	Positive	NS	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive
Serology		IgM/IgG SARS-Cov-2 antibodies Weakly positive					IgG SARS-Cov-2 Antibodies Positive				

Table 1 continued

Author	Serzan *et al.*, 2020[1]	Lovly *et al.*, 2020[2]	Szabados *et al.*, 2020[3]				Schmidle *et al*, 2020[4]	Artigas *et al.*, 2020[5]	Bonomi *et al.*, 2020[6]	Yekedüz *et al.*, 2020[7]	O'Kelly *et al.*, 2020[8]
Treatment	High-dose corticosteroids, tapered when swab result was positive; nivolumab monotherapy initiated	Methylprednisolone 1 g/day for 2 days; prednisolone 1 mg/kg; prednisolone 2 mg/kg; infliximab 5 mg/mg; vancomycin; piperacillin/ tazobactam; immunoglobulins 1 g/kg; steroids weaned; mechanical ventilation; hypoxaemic respiratory; failure; PD-L1 increased in alveolar walls where viral DNA was detected; IgG response suggested infection before immunotherapy and chemotherapy	High-flow oxygen; co-amoxiclav; clarithromycin	Self-isolation	Self-isolation	Volume replacement; PIP/TAZ	Supportive	PIP/TAZ;HCQ	Oxygen; antibiotics	Oxygen; PIP/TAZ; oseltamivir; clarithromycin; metronidazole; azithromycin; HCQ. When CT showed ground-glass opacities, favipravir added	Oxygen; PIP/TAZ; doxycycline; lopinavir; ritonavir; HCQ; azithromycin; lopinavir/ritonavir stopped
ICI treatment	Nivolumab resumed then discontinued after CR	IT discontinued	IT not yet recommenced	IT recommenced	IT recommenced	IT recommenced	NS	NS	NA	NA	NS
Outcome	Alive	Dead	Alive	Alive	Alive	Alive	Alive	Not specified	Dead	Dead	Alive

COPD, chronic obstructive pulmonary disease; CR, complete response; CT, computed tomography; CXR, chest X-ray; HCQ, hydroxychloroquine; ICI, immune checkpoint inhibitor; irAE, immune-related adverse event; IT, immunotherapy; NA, not applicable; NS, not stated; PD-L1, programmed death ligand-1; PIP/TAZ, piperacillin/tazobactam.

1. Serzan MT, Kumar PN, Atkins MB. Diffuse pneumonitis from coronavirus HKU1 on checkpoint inhibitor therapy. *J Immunother Cancer* 2020; **8:** e000898. 2. Lovly CM, Boyd KL, Gonzalez-Ericsson PI *et al.* Rapidly fatal pneumonitis from immunotherapy and concurrent SARS-CoV-2 infection in a patient with newly diagnosed lung cancer. *medRxiv* 2020; https://doi.org/10.1101/2020.04.29.20085738; 3. Szabados B, Abu-Ghanem Y, Grant M *et al.* Clinical characteristics and outcome for four SARS-CoV-2-infected cancer patients treated with immune checkpoint inhibitors. *Eur Urol* 2020; **78:** 276–80. 4. Schmidle P, Biedermann T, Posch C. COVID-19 in a melanoma patient under treatment with checkpoint-inhibition. *J Eur Acad Dermatol Venereol* 2020; https://doi.org/10.1111/jdv.16661. 5. Artigas C, Lemort M, Mestrez F *et al.* COVID-19 pneumonia mimicking immunotherapy-induced pneumonitis on 18F-FDG PET/CT in a patient under treatment with nivolumab. *Clin Nucl Med* 2020; **45:** e381–2. 6. Bonomi L, Ghilardi L, Arnoldi E *et al.* A rapid fatal evolution of coronavirus disease-19 in a patient with advanced lung cancer with a long-time response to nivolumab. *J Thorac Oncol* 2020; **15:** e8–5. 7. Yekedüz E, Dursun B, Aydın GÇ *et al.* Clinical course of COVID-19 infection in elderly patient with melanoma on nivolumab. *J Oncol Pharm Pract* 2020; **26:** 1289–94. 8. O'Kelly B, McGettrick P, Angelov D *et al.* Outcome of a patient with refractory Hodgkin lymphoma on pembrolizumab, infected with SARS-CoV-2. *Br J Haematol* 2020; 190: e1–3.

enabling clinicians to counsel their patients adequately. Furthermore, in light of the apparent increased mortality in various ethnic groups,[5,6] combined with the potential under-reporting of ethnicity in the published COVID-19 dermatological literature,[7] a register would ensure that key risk factors are not overlooked. In the absence of this information, it seems prudent to thoroughly assess all patients due to commence, and those currently undergoing, immune checkpoint therapy, for coronavirus risk factors and symptoms, complemented by early and rigorous SARS-CoV-2 PCR testing where clinically indicated and available.

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References

1 Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2019.
2 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.
3 Lee LYW, Cazier JB, Starkey T *et al*. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. *Lancet* 2020; **395**: 1919–26.
4 Bersanelli M. Controversies about COVID-19 and anticancer treatment with immune checkpoint inhibitors. *Immunotherapy* 2020; **12**: 269–73.
5 Niedzwiedz CL, O'Donnell CA, Jani BD *et al*. Ethnic and socioeconomic differences in SARS-CoV-2 infection: prospective cohort study using UK Biobank. *BMC Med* 2020; **18**: 160.
6 de Lusignan S, Dorward J, Correa A *et al*. Risk factors for SARS-CoV-2 among patients in the Oxford Royal College of General Practitioners Research and Surveillance Centre primary care network: a cross-sectional study. *Lancet Infect Dis* 2020; **6**: e18606. https://doi.org/10.2196/18606
7 Lester JC, Jia JL, Zhang L *et al*. Absence of skin of colour images in publications of COVID-19 skin manifestations. *Br J Dermatol* 2020.

Patient perceptions of Mohs micrographic surgery during the COVID-19 pandemic and lessons for the next outbreak

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Understanding patient experiences of healthcare systems during the pandemic is important to help strategize for future similar events. We operated a reduced Mohs micrographic surgery (MMS) service during the pandemic by rationalizing patients by tumour type, age, comorbidities and patient choice. We sought to establish patient expectations and concerns of attending for MMS by conducting a survey of those attending surgery over a 7-week period from 24 April 2020. The results are particularly relevant when re-establishing services in preparation for an expected upsurge of routine activity (including surgical procedures) or 'second spike' of COVID-19 cases later this year.

Although patients who may not have attended surgery were not surveyed, 37% of patients had at least one risk factor for COVID-19 and 27% were over the age of 70 years. Furthermore, we also had a high response rate of 96% (151 responses) reflecting an accurate representation of patient experiences.

Of the survey respondents, 52% were male and 48% female and the majority (98%) white. The age range was 30–89 years and the majority (91%) described their health status as good to excellent.

Our main findings were that the overwhelming majority of patients (82%) were relieved to have surgery. Nearly half (47%) had been worried the hospital would cancel their surgery. Only 17% considered cancelling due to concerns about contracting coronavirus, transmitting to household/family members, or taking public transport, although 54% were anxious about using public transport to attend their appointment. The overwhelming majority (80%) stated they would normally have used public transport if there was not an ongoing pandemic, but only 45% actually did.

Less than a quarter were concerned they would contract COVID-19 in hospital and 30% were concerned about transmitting to household/family members. Only 19% were concerned about the ability to social distance in hospital. Despite these concerns, patients still attended for MMS.

To our knowledge, this is the first study exploring patient perceptions of MMS during the pandemic. Patients overwhelmingly appreciated having MMS treatment in a safe environment. There were some COVID-19-related concerns; however, patients felt that attending their appointment was more important. Relatively few patients were concerned about being able to socially distance in hospital; this may reflect our strong infection-control measures[1] and effective communication, including a nurse-led consultation prior to the appointment. During this consultation, patients were given information about