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.

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Letter to the Editor

Duration of isolation and precautions in immunocompromised patients with COVID-19

Sir,

Current international guidelines recommend, for most persons with COVID-19 illness, discontinuation of isolation and precautions after 10 days from the onset of symptoms and after at least 24 h without fever [1]. A longer period of isolation, up to 20 days after symptom onset, is recommended for patients with severe illness. The lack of infectivity in people with duration of symptoms >20 days has important implications for public health policy and in hospital infection control. However, these indications might not apply to immunocompromised patients, who might require more time to obtain viral clearance [2]. For this reason, in such a population, the correct timing of isolation is yet to be ascertained. We therefore wanted to report our experience and the results of literature review focused on prolonged shedding of a viable virus in immunocompromised patients.

We report three cases of immunocompromised patients cared for in our Infectious Disease Unit in Northern Italy — Policlinic IRCCS San Martino University Hospital, Genoa — two with haematologic malignancies and one with rituximab-treated neuromyelitis optica (Table I), all with persistent reverse transcription—polymerase chain reaction (RT—PCR) positivity in nasopharyngeal swabs after weeks or months from the diagnosis of SARS-CoV-2 infection. These patients had viable virus isolated (cytopathic effect in Vero E6 cells at 48 or 72 h), 238, 37, and 40 days after the first RT—PCR positivity (Allplex 2019 nCOV Seegene — Three Target assay towards genes Envelope/Polymerase/Nucleocapsid, E/RdRp/N).

The literature review identified other ten cases of immunocompromised patients in whom viable virus was cultured more than 10 days after the onset of infection, and, in most cases, also after more than 20 days (median: 46.5 days; range: 17—119; Table I). Of note, not only did severely ill patients have a prolonged shedding of viable virus, but also those with mild or asymptomatic infection.

These results advocate for customized public health policies and hospital infection control differentiation, not only based on the severity of COVID-19 illness, but also considering the baseline comorbid conditions and immune competence of the patients. A possible approach could be a test-based (PCR or antigen) strategy, as proposed for some cases of severely immunocompromised patients by the Centers for Disease Control and Prevention (CDC) [1]. However, it should be noted that intermittent negativity of molecular tests has also been reported for immunosuppressed patients and that, as a consequence, the test-based approach might also have gaps [8,9]. Moreover, a shared definition of when considering persons 'severely immunocompromised' is not provided by CDC indications, while a prolonged shedding of viable SARS-CoV-2 virus has also been reported outside the settings of haematological malignancies or solid organ transplantation [1,3,8]. Finally, some patients with a positive PCR result might not shed a viable virus, thus prolonging isolation might not be necessary.

In conclusion, special attention should be given to isolation precautions in immunocompromised people with SARS-CoV-2 infection, especially in hospital settings, even if only mild symptoms are present. A longer time-period should be considered before discontinuing precautions than in the immunocompetent, and viral culture might be useful to determine potential contagiousness of people with prolonged RT—PCR positivity in nasopharyngeal swabs.

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Table I

Patients' characteristics at the time of the last positive nasopharyngeal swab with documented viable virus and review of the literature including published cases of patients with haematological malignancies and viable virus after more than 10 days from symptoms onset

Patient group	Patient ID, Reference	Age (years)	Sex	Baseline condition	Clinical manifestation of SARS-CoV-2	Days from SARS-COV-2 diagnosis	Gene tested and RT—PCR cycle at positivity	Viraemia	SARS-CoV-2 Vero cell infectivity
Patients followed up in Genoa	1	70	M	Mantle cell lymphoma treated with R-BAC	Pneumonia and respiratory failure	238	E/RdRp/N 22/22/22	Positive	Yes
	2	50	F	Neuromyelitis Optica on rituximab	Pneumonia and respiratory failure	37	E/RdRp/N 28/29/28	Positive	Yes
	3	47	F	IgA multiple myeloma with CNS localizations on D-PACE	Pneumonia without respiratory failure	40	E/RdRp/N 19/18/20	Negative	Yes
Patients described in the literature	Baang *et al.* [3]	70	M	Mantle cell lymphoma on mosunetuzumab + cyclophosphamide, doxorubicin, prednisone, and polatuzumab vedotin	Pneumonia and respiratory failure	119	S/Orf1ab 21.5/21.3	NA	Yes
	MSK3, Aydillo *et al.* [4]	NA	NA	HSCT/CAR-T-cell therapy[a]	NA	25	NA	NA	Yes
	MSK4, Aydillo *et al.* [4]	NA	NA	HSCT/CAR-T-cell therapy[a]	NA	26	NA	NA	Yes
	MSK6, Aydillo *et al.* [4]	NA	NA	HSCT/CAR-T-cell therapy[a]	NA	61	NA	NA	Yes
	MSK8, Aydillo *et al.* [4]	NA	NA	Haematological malignany not futher defined[a]	NA	17	NA	NA	Yes
	Nakajima *et al.* [5]	47	M	Follicular lymphoma treated with obinutuzumab plus bendamustine	Pneumonia without respiratory failure	59	NA[b]	NA	Yes
	Avanzato *et al.* [6]	71	F	Chronic lymphocytic leukaemia and hypogammaglobulinaemia treated with IVIG	Absence of respiratory symptoms	49 70	E 28 E 22	NA	Yes
	Decker *et al.* [7]	62	M	Heart transplantation on cyclosporine, mycophenolate, and prednisone	Absence of respiratory symptoms	18 21	NA	NA	Yes
	Guetl *et al.* [8]	NA	NA	X-linked agammaglobulinaemia	Pneumonia and respiratory failure	44	25	NA	Yes
	Choi *et al.* [9]	45	M	Antiphospholipid syndrome on glucocorticoids, cyclophosphamide, rituximab, and eculizumab	Pneumonia and respiratory failure	72 143	Orf1ab 27.6 Orf1ab 15.6	NA NA	Yes (day 75) Yes

R-BAC, rituximab, bendamustine and cytarabine; E, envelope gene; RdRp, polymerase gene; N, nucleocapsid protein gene; CNS, central nervous system; D-PACE, cisplatin, doxorubicin, cyclophosphamide, etoposide; S, spike protein gene; Orf1ab, open reading frame 1a and 1b; HSCT, haematopoietic stem cell transplantation; CAR-T-cell, chimeric-antigen-receptor (CAR)-T-cell; IVIG, intravenous immunoglobulins; NA, not available.

[a] Only aggregated data were available for the cases cited.

[b] 1.2×10^4 copies/assays.

Conflict of interest statement
None declared.

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