Response to: 'Correspondence on 'What comes after the lockdown? Clustering of ANCA-associated vasculitis: single-centre observation of a spatiotemporal pattern" by Hocevar *et al*

In our previous report on antineutrophil cytoplasm antibodies (ANCA)-associated vasculitides (AAV) during the current COVID-19 pandemic, we described our observation of both an incidence-shift with a post-lockdown clustering and an increased incidence rate of AAV diagnoses between February and August 2020 compared with previous years.[1]

In correspondence to our article, Hocevar *et al* report how COVID-19 pandemic affected management of patients with vasculitides at their centre. The in-depth analysis examined symptom duration (ie, time eclipsed to final diagnosis), disease activity/severity and seasonal changes of patients presenting with giant cell arteritis, and IgA vasculitis and AAV during 2020 and in the previous decade. No significant differences were found in incidence rates or indications for deferrals; that is, symptoms were experienced for a longer length of time before a diagnosis was made or a more severe presentation occurred.[2]

As the COVID-19 pandemic remains ongoing, six patients with AAV treated at our centre contracted COVID-19; clinical details are summarised in table 1. One patient (patient 2) on maintenance rituximab required intensive care unit treatment, while another with a recent disease relapse (patient 1) was hospitalised. Moderate hypogammaglobulinaemia was detected in these patients. The remaining four patients were not admitted and managed as outpatients. Patient 1 received rituximab induction therapy 2 months before COVID-19 and due to active disease on kidney biopsy, was receiving intravenous cyclophosphamide (cumulative dose >3 g) just before SARS-CoV-2 infection. Patient 2 was admitted to the intensive care unit and received non-invasive ventilation for several days, alongside remdesivir, dexamethasone and convalescent plasma (two doses). Nonetheless, he had undetectable SARS-CoV-2 antibodies after discharge. Outcomes were favourable in all six patients. All but one patient underwent SARS-CoV-2 antibody testing following COVID-19, and antibodies were detectable in three of five patients.

There is consensus that active disease and relapses need to be prevented and managed appropriately, but great uncertainty remains with regards to several crucial questions. Due to its favourable efficacy and safety profile, rituximab is the standard treatment for induction and maintenance treatment of patients with AAV. Yet increasing evidence suggests rituximab treatment itself is a risk factor for unfavourable outcomes of COVID-19 in patients with autoimmune diseases,[3] and a diagnosis of vasculitis might confer a particular risk. No information, however, was provided about concomitant disease activity, as these patients may be at risk for worse prognosis.

Furthermore, long-term B cell depletion hinders adequate immune response to both infection control and vaccination. Absence of SARS-CoV-2 antibodies following COVID-19 in rituximab users may be frequent and as such, places patients at risk of reinfection.[4] The most pressing question related to rituximab use and COVID-19 is vaccine readiness; that is, predicting an adequate immune response following administration of COVID-19 vaccines.[5 6] Production of antibodies against the S1-protein of the virus and neutralising antibodies might be diminished or absent when patients are vaccinated within the first weeks following the last rituximab dose. Tools to measure T cell immunity in such situations should be implemented to potentially predict a protective effect of vaccination despite absent humoral response.

While the pandemic is an ongoing challenge for patients and physicians, research into vaccine response and risk factors for COVID-19-related mortality continues. Such investigations will inform physicians of vaccine response in several circumstances (eg, ongoing high doses steroids, impact of disease activity, and ultimately, if a T cell response is sufficient to reduce severity of COVID-19). Effective combatting in the pandemic necessitates flexible approaches to patient management, such as telemedicine and the potential use of alternative treatments, as well as the continued vaccination of our vulnerable patient groups.

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Table 1 Six patients with antineutrophil cytoplasm antibodies-associated vasculitis contracted COVID-19

Patient	Age	Sex	Induction therapy	Maintenance therapy	Immunsuppression (within the last 6 months)	Admission to hospital	Serum creatinine (mg/dL) before COVID-19	Hypogammaglobulinaemia	COVID-19 renal outcome	COVID-19 overall outcome	Serum creatinine (mg/dL) after COVID-19	SARS-CoV-2 antibodies
1	72	M	Yes	–	Cyclophosphamide 3.09 g (3 pulses), rituximab (2×1 g), methylprednisolone (3.06 g)	Yes	3.30	Moderate (IgG 336 mg/dL)	AKI (peak creatinine 5.12)	Oxygen supply (max. 4 L), steroids increased	2.45	Detectable
2	62	M	–	Yes	Rituximab (1 g)	Yes	1.19	Moderate (IgG 409 mg/dL)	AKI (peak creatinine 1.73)	Non-invasive ventilation, remdesivir, dexamethasone, convalescent plasma	1.38	Not detectable
3	61	M	–	–	–	No	1.35	No (IgG 1150 mg/dL)	–	Home quarantine	1.29	–
4	80	F	–	–	–	No	3.06	No (IgG 1100 mg/dL)	–	Home quarantine	2.33	Detectable
5	56	F	–	–	–	No	0.86	No (IgG 705 mg/dL)	–	Home quarantine	0.84	Detectable
6	39	F	–	Yes	Rituximab (1 g)	No	0.75	No (IgG 1120 mg/dL)	–	Home quarantine	0.75	not detectable

AKI, acute kidney injury; F, female; M, male.

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Ethics approval IRB approval of our study was obtained (No. 1215/2020, Medical University Innsbruck).

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