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.

Glomerular basement membrane nephritis: crescentic renal inflammation and immunosuppressive intervention in the time of the severe acute respiratory syndrome coronavirus 2 pandemic

To the editor: The diagnosis and management of autoimmune disorders is challenging in the current pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Here, we describe the case of a patient with anti–glomerular basement membrane (GBM) disease complicated by a SARS-CoV-2 infection to highlight the importance of appropriate immunosuppression and individualized care in respect of these 2 disease processes.

The 44-year-old Caucasian male presented to the emergency department with palpitations and a new tickling cough. He displayed tachycardia, lymphopenia (0.21 × 10^9/L), and a positive rapid test for SARS-CoV-2. He recently had been diagnosed with anti-GBM glomerulonephritis (GN), causing an acute kidney injury. He was receiving alternate-day plasma exchange, oral glucocorticoids, and i.v. cyclophosphamide pulses to preserve kidney function. His chest radiography did not reveal any pneumonic consolidation. He was admitted to the hospital and commenced on remdesivir. He did not develop more severe symptoms of pneumonitis typical for SARS-CoV-2. After 5 days of remdesivir treatment, he was discharged and his plasma exchange and cyclophosphamide therapies were restarted while he remained SARS-CoV-2 polymerase chain reaction (PCR)–positive. SARS-CoV-2 PCR became undetectable after a total of 31 days, and SARS-CoV-2 antibodies were detected (Figure 1).

The current pandemic is a global health threat and a great challenge to vasculitis and GN care. Here, we describe a SARS-CoV-2 infection in a vasculitis patient in which the viral infection remained mild despite aggressive immunotherapy. A registry of SARS-CoV-2 infection in patients with immune-mediated kidney diseases proposed a higher mortality in GN patients.[1] Waldman *et al.* detected a higher rate of acute kidney injury and a more pronounced hypoalbuminaemia in 40 GN patients as potential causes for the adverse outcome, while the immunotherapy did not correlate with mortality. Risk stratification in SARS-CoV-2 disease is evolving.[2–4] SARS-CoV-2 vaccination will be the most important step toward

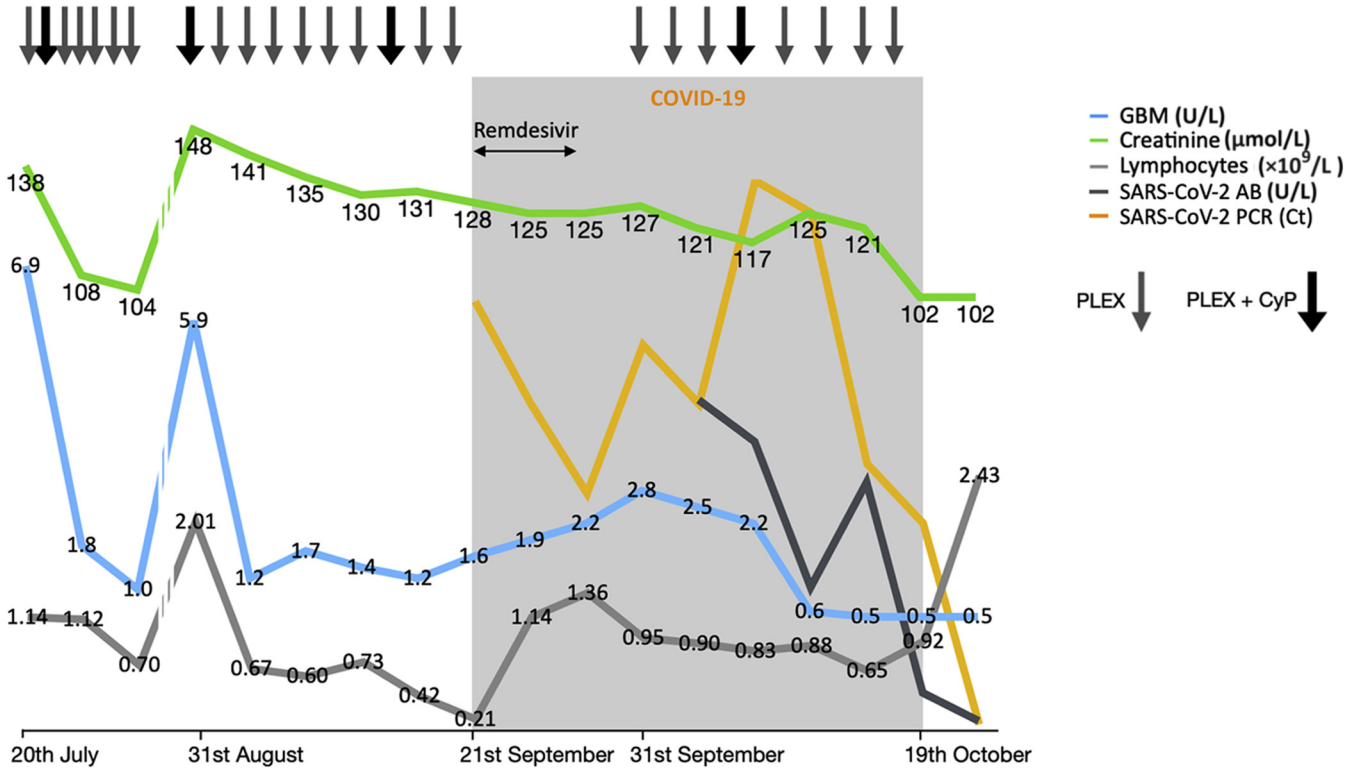

Figure 1 | Induction immunotherapy for anti–glomerular basement membrane (GBM) disease complicated by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Patient received plasma exchange (PLEX) and i.v. cyclophosphamide (CyP) pulse therapy and oral prednisolone. Depicted are his GBM antibody level (U/L), renal function (creatinine in µmol/L), lymphocyte count (×10^9/L), SARS-CoV-2 quantitative polymerase chain reaction (PCR) in million viral copies/swab, and antibody (AB) levels (ratio/index).

protecting immune-compromised patients. In the presence of scarce resources, equitable and effective risk–benefit allocation will be vital, prioritizing vulnerable patients. Timing immunotherapy with vaccination and determining vaccination response will be crucial. Concurrent SARS-CoV-2 infection should not prevent delivery of effective immunomodulatory therapy in patients with severe autoimmune diseases, essential for the protection and recovery of vital organ function.

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Silke R. Brix[1], Rachel B. Jones[2] and David R.W. Jayne[2]

[1]Renal, Urology and Transplantation Unit, Manchester University Hospitals, Manchester, UK; and [2]Vasculitis and Lupus Clinic, Addenbrooke's Hospital, Cambridge, UK

Correspondence: *Silke R. Brix, Renal, Urology and Transplantation Unit, Manchester Royal Infirmary, Manchester University Hospitals NHS Foundation Trust, Manchester, UK. E-mail: silke.brix@mft.nhs.uk*

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Kidney disorders as serious adverse drug reactions of remdesivir in coronavirus disease 2019: a retrospective case–noncase study

To the editor Remdesivir is a novel adenosine-like nucleotide analogue, representing the first drug approved for coronavirus disease 2019 (COVID-19), albeit an uncertain clinical relevance. In clinical trials and case series, acute kidney injury (AKI), including renal replacement, has been frequently reported.[1,2] Although causality is debatable, kidney injuries, especially proximal tubular epithelial cell necrosis, have also been observed in animal studies during remdesivir development.

To provide additional data, we performed a pharmacovigilance analysis on the World Health Organization global database of individual case safety reports, VigiBase (https://www.who-umc.org/vigibase/vigibase/). This database gathers spontaneous reports of suspected adverse drug reactions from >130 countries, which makes it a powerful tool to perform disproportionality analyses.[3] This approach, based on a case–noncase method, estimates whether an adverse event is differentially reported for a specific drug compared with other drugs.

Among 1,565,117 reports registered from January 1st until August 30th, 2020, 5532 concerned COVID-19 patients and have been included in this study. Of them, 434 (7.8%) cases were related to kidney disorders, including 327 (5.9%) reported with remdesivir. In remdesivir kidney disorder cases, 217 (66.3%) patients were male, with a median age of 65 (interquartile range, 55–73) years (Supplementary Table S1). Remdesivir was discontinued early after kidney disorder onset, with a median treatment duration of 3 (interquartile range, 1–4) days. In the vast majority of cases (316 [96.6%]), no other drug was suspected in the onset of

Table 1 | Reporting of kidney disorders in remdesivir users among COVID-19 patients, and their RORs within the WHO global pharmacovigilance database

Type of analysis	Kidney disorder cases[a]	Noncases[b]	ROR (95% CI)
Primary analysis			
Remdesivir users	327	1526	7.2 (5.7–9.0)
Other drug users	107	3572	1 (Reference)
Sensitivity analysis restricted to severe to critical COVID-19 patients			
Remdesivir users	327	1526	3.7 (2.6–5.4)
Dexamethasone, sarilumab, or tocilizumab users	34	591	1 (Reference)
Sensitivity analysis restricted to serious kidney disorders[c]			
Remdesivir users	301	1552	6.9 (5.4–8.7)
Other drug users	101	3578	1 (Reference)
Sensitivity analysis restricted to kidney disorders not including concomitant nephrotoxic drugs[d]			
Remdesivir users	242	1611	6.1 (4.8–7.9)
Other drug users	88	3591	1 (Reference)

CI, confidence interval; COVID-19, coronavirus disease 2019; ROR, reporting odds ratio; WHO, World Health Organization.

The case–noncase approach is similar to case-control method but for purpose of pharmacovigilance studies. Disproportionality in adverse drug reaction reporting between groups is expressed using RORs and their 95% CIs. ROR is a ratio similar in concept to the odds ratio in case-control studies and corresponds to the exposure odds among reported cases of kidney disorders over the exposure odds among reported noncases. An ROR >1 suggests that kidney disorders are more frequently reported in remdesivir users compared with other drug users (i.e., chloroquine, hydroxychloroquine, dexamethasone, lopinavir/ritonavir, sarilumab, or tocilizumab users) among patients with COVID-19 (list of terms is provided in the Supplementary Data). Reports with remdesivir that also included any other drug mentioned above were further excluded (corresponding to 806 reports). To assess the robustness of the main analysis, we performed several sensitivity analyses. First, to take into account clinical patient status and intensive care unit settings, we further restricted the analysis to drugs specifically used in severe to critical COVID-19 patients (i.e., dexamethasone, sarilumab, or tocilizumab). Second, we restricted the analysis to (i) serious kidney disorder cases only and (ii) kidney disorder cases that did not include known concomitant nephrotoxic drugs. In sensitivity analyses, nonserious cases and cases including concomitant nephrotoxic drugs were considered as noncases.

[a]Kidney disorder cases were individual case safety reports containing any reaction belonging to the kidney system as system organ class, according to the Medical Dictionary for Regulatory Activities (https://www.meddra.org/).

[b]Noncases were reports containing any other reaction.

[c]Serious cases were defined, according to the WHO, as the occurrence of death, life-threatening adverse event, inpatient hospitalization or prolongation of an existing hospitalization, significant disability, or requirement of intervention to prevent any of these.

[d]List of concomitant or suspected nephrotoxic drugs is in the Supplementary Data.