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COVID-19 therapeutic options for patients with kidney disease

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To the editor: Viral diseases are among the leading causes of morbidity and mortality in the world.[1] A novel coronavirus, designated as COVID-19, recently emerged in Wuhan, China, at the end of 2019. As of March 5, 2020, there are >95,000 reported cases of COVID-19 and >3,000 deaths wordwide.[2] Given the race against time, identifying drug treatment options as soon as possible is critical to adequately respond to the COVID-19 outbreak.[3]

The "one drug, multiple viruses" paradigm came with the discovery of broad-spectrum antiviral agents, small molecules that inhibit a wide range of human viruses,[1] and is even more pertinent today with outbreaks of Ebola, Zika, Dengue, influenza, and other viral infections, especially COVID-19. Because COVID-19 is 75% to 80% identical to the severe acute respiratory syndrome–CoV and even more closely related to several bat coronaviruses,[4] potential treatment options against this emerging virus include as lopinavir/ritonavir, nucleoside analogues, neuraminidase inhibitors, remdesivir, fusion peptide (EK1), abidol, RNA synthesis inhibitors (such as tenofovir disoproxil fumarate [TDF], lamivudine [3TC]), interferon-α, and Chinese traditional medicine, such Shufengjiedu capsules and Lianhuaqingwen capsules, are. However, the efficacy and safety of these drugs for COVID-19 require confirmation by clinical experiments.[3]

Chronic kidney disease (CKD) is frequently encountered in the general population and is a risk for increased viral morbidity. According to the U.S. Centers for Disease Control and Prevention, approximately 15% of U.S. adults (37 million people) are estimated to have CKD.[5] During the first 2 months of the current outbreak in China, CKD was reported in 4.3% of the Chinese patients infected with COVID-19 who had severe presentation.[6] End-stage kidney disease patients are a highly susceptible group with an infection rate of 16%, which exceeds that observed in other populations.[7]

In the context of the epidemic or pandemic of COVID-19, these drugs will be prescribed to patients with CKD and/or

Table 1 | Drug treatment options for COVID-19: potential kidney damage and dosage adjustment in CKD patients

	COVID-19 status	Dosage according to glomerular filtration rate	Renal adverse events
Nucleoside analogs			
Favipiravir	Phase II	Not available[a]	Not reported
Remdesivir	Phase III		Potential mitochondrial toxicity
Galidesivir	Animal		
Azvudine	Phase II		
Ribavirin (in combination)	Phase II	Dosage adjustment according to standard recommendation Drug may be administered regardless of hemodialysis schedule	Not reported Hyperuricemia due to hemolytic anemia
Neuraminidase inhibitors			
Oseltamivir (in combination)	Phase IV	Dosage adjustment according to standard recommendation Drug should be administered after dialysis session to avoid drug loss	Not reported
Fusion peptide inhibitor			
EK1	Cell culture	—	—
HIV protease inhibitor			
Lopinavir/ritonavir	Phase IV/III	Drug should be administered at normal dosage and regardless of hemodialysis schedule	Reversible AKI
Danoprevir (in combination)	Phase IV	Not available[a]	Not reported
Darunavir + cobicistat	Phase II/III	Drug may be administered at normal dosage and regardless of hemodialysis schedule	Nephrolithiasis False creatinine level increase
Membrane fusion inhibitor			
Umifenovir	Phase IV	Not available[a]	Not reported
Aminoquinoline family			
Chloroquine	Phase IV	Dosage adjustment according to standard recommendation	Renal lipidosis mimicking Fabry disease
Hydroxychloroquine	Phase III	Drug should be administered after session on hemodialysis days	Renal lipidosis mimicking Fabry disease False proteinuria
Immunotherapy			
Camrelizumab	Phase II	Not available[a]	Not yet reported Potential PDL-1 ligand-like renal toxicity

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Table 1 | (Continued) **Drug treatment options for COVID-19: potential kidney damage and dosage adjustment in CKD patients**

	COVID-19 status	Dosage according to glomerular filtration rate	Renal adverse events
Monoclonal antibodies			
Adalimumab	Phase IV	Drug should be administered at normal dosage[a]	Autoimmune GN (MN, IgA, lupus, ANCA vasculitis); granulomatous AIN
Tocilizumab	Phase IV		Not reported
Bevacizumab	Phase II/III	Drug should be administered at normal dosage and regardless of hemodialysis schedule	HT, proteinuria, TMA, GN, IN
IFX-1 Anti C5a	Phase II	Not available[a]	Not reported
Leronlimab	Phase II		
REGN-3048, REGN-3051	Phase I		
VelocImmune (Regeneron Technology, Tarrytown, NY)	Phase I		
Others			
Tenofovir alafenamide	Phase IV	Dosage adjustment according to standard recommendation	AKI; proximal renal tubular acidosis
Thalidomide	Phase II	Drug should be administered after dialysis session	Hyperkalemia
Ig	Phase II/III	Drug should be administered at normal dosage In the absence of hemodialysis clearance data, drug should be administered after session on hemodialysis days	AKI; osmotic nephrosis
Pirfenidone	Phase III	Not available[a]	Not reported
Tranilast	Phase IV		Not reported
Fingolimod	Phase II	Drug should be administered at normal dosage and regardless of hemodialysis schedule	TMA
Leflunomide	Phase III		Anti-GBM GN; HT; tubular renal acidosis; TMA (in combination with methotrexate)
Artemisinin piperaquine	Phase IV	Not available[a]	AKI; fatal acute hepatorenal failure

COVID-19, novel coronavirus disease 2019; AIN, acute interstitial nephritis; AKI, acute kidney injury; ANCA, antineutrophil cytoplasmic antibody; CKD, chronic kidney disease; GN, glomerulonephritis; GBM, glomerular basement membrane; HT, hypertension; IN, interstitial nephritis; MN, membranous nephropathy; PDL-1, programmed death ligand 1; TMA, thrombotic microangiopathy.
[a]In the absence of hemodialysis clearance data, drug should be administered after session on hemodialysis days.

end-stage kidney disease. Clinicians should thus be aware of the potential dosage adjustments and renal adverse events of those drugs in this patient group (Table 1).

Through this letter, we are not advocating any specific therapy and we support the notion that any therapy requires evaluation in a clinical trial. Furthermore, the rationale for providing this information to nephrologists is that we are likely to see off-label use of these drugs despite the absence of data, and we will need to provide input as to how the dosing should be modified in our patients with severely impaired kidney function.

DISCLOSURE

KDJ serves as a consultant for Astex Pharmaceuticals. All the other authors declared no competing interests.

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