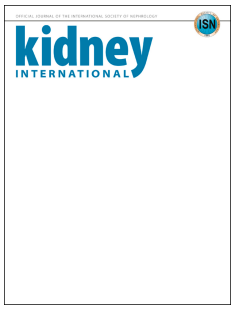

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Hassan Izzedine, MD. PhD, Kenar D. Jhaveri, MD, PhD, Mark A. Perazella, MD

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2019-nCoV therapeutic options for patients with Kidney Disease

Hassan Izzedine[1], MD. PhD, Kenar D. Jhaveri[2], MD, PhD, Mark A Perazella[3], MD

[1]Department of Nephrology, Peupliers Private Hospital, Ramsay Générale de Santé, Paris, France.
[2]Division of Kidney Diseases and Hypertension, Donald and Barbara School of Medicine at Hofstra/100 Community Drive, Great Neck, NY 11021.
[3]Yale University School of Medicine, New Haven, CT 06520, USA

kjhaveri@northwell.edu
mark.perazella@yale.edu
h.izzedine@ramsaygds.fr

Corresponding Author: Hassan Izzedine
h.izzedine@ramsaygds.fr
tel: +33 1 44 16 52 01
Fax: +33 1 44 16 55 94

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Sir,

Viral diseases are one of the leading causes of morbidity and mortality in the world.[1] A novel coronavirus, designated as 2019-nCoV, recently emerged in Wuhan, China, at the end of 2019. As of March 5, 2020, there are more than 95 thousand reported cases of COVID-19, and greater then 3000 deaths wordwide.[2] Given the race against time, identifying drug treatment options as soon as possible is critical to adequately respond to the 2019-nCoV outbreak.[3]

The "one drug, multiple viruses" paradigm came with the discovery of broad-spectrum antiviral agents (BSAAs), small-molecules that inhibit a wide range of human viruses[1] is even more pertinent today with outbreaks of Ebola, Zika, Dengue, influenza and other viral infections, especially the 2019-nCoV. Since 2019-nCoV is 75 to 80% identical to the SARS-CoV and even more closely related to several bat coronaviruses[4], molecules such as Lopinavir/Ritonavir, Nucleoside analogues, Neuraminidase inhibitors, Remdesivir, fusion peptide (EK1), abidol, RNA synthesis inhibitors (such as TDF, 3TC), IFN-alpha, Chinese traditional medicine, such ShuFengJieDu Capsules and Lianhuaqingwen capsule, are potential treatment options against this emerging virus. However, the efficacy and safety of these drugs for 2019-nCoV 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. Approximately 15% of US adults (37 million people) are estimated to have CKD [https://www.cdc.gov/kidneydisease/publications-resources/2019-national-facts.html]. During the first 2 months of the current outbreak in China, CKD was reported in 4.3% of the 2019-nCov Chinese infected-patients with severe presentation.[5] End-stage kidney disease patients are a highly susceptible group with an infection rate of 16%, which exceeds that observed in other populations [https://www.medrxiv.org/content/10.1101/2020.02.24.20027201v2].

In the context of the epidemic or pandemic of 2019-nCoV, these drugs will be prescribed to CKD and/or ESKD patients. Clinicians should thus be aware of the potential dosage adjustments and renal adverse events of those drugs in this patient group (table 1).

Table 1. Drug treatment options for the 2019-nCoV: potential kidney damage and dosage adjustment in CKD patients

	2019-nCoV Status	Dosage according to glomerular filtration rate	Renal adverse events
Nucleoside analogs			
Favipiravir	Phase II	Not available*	Not reported Potential mitochondrial toxicity
Remdesivir	Phase III		
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*	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*	Not reported
Aminoquinoline family			
Chloroquine	Phase IV	Dosage adjustment according to standard recommendation Drug should be administered after session on hemodialysis days	Renal lipidosis mimicking Fabry disease
Hydroxychloroquine	Phase III		Renal lipidosis mimicking Fabry disease False proteinuria
Immunotherapy			
Camrelizumab	Phase II	Not available*	Not yet reported Potential PDL-1 ligand like renal toxicity
Monoclonal antibodies			
Adalimumab	Phase IV	Drug should be administered at normal dosage.*	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, NI
IFX-1 Anti C5a	Phase II	Not available*	Not reported
Leronlimab	Phase II		
REGN-3048, REGN-3051	Phase I		
VelocImmune	Phase I		
Others			
Tenofovir Alafenamide	Phase IV	Dosage adjustment according to standard recommendation. Drug should be administered after dialysis session	AKI. Proximal renal tubular acidosis
Thalidomide	Phase II		Hyperkalemia
Immunoglobulin	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
Pirfrnidone	Phase III	Not available*	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)
Artemisinine Piparequine	Phase IV	Not available*	AKI. Fatal acute hepatorenal failure

* In the absence of hemodialysis clearance data, drug should be administered after session on hemodialysis days.

Abbreviations: CKD, chronic kidney disease; AKI, acute kidney injury; GN, glomerulonephritis; AIN, acute interstitial nephritis; HT, hypertension; TMA, thrombotic microangiopathy; GBM, glomerular basement membrane.

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