

The Medical Letter

Essential to your practice

The Medical Letter on Drugs and Therapeutics

ISSUE April 6, 2020

1595

1. **Some Drugs for COVID-19**
2. **Two Drugs for Sickle Cell Disease: Crizanlizumab (Adakveo) and Voxelotor (Oxbryta)**
3. **Bempedoic Acid (Nexletol) for Lowering LDL-Cholesterol**
4. **Intravenous Cetirizine (Quzyttir) for Acute Urticaria**

Some Drugs for COVID-19

Med Lett Drugs Ther. 2020 Apr 6;62(1595):49-56

Last updated: March 27, 2020 (this article will be continuously updated as more information becomes available).

Read our blog post on this topic: [Remdesivir: A Possible Treatment for 2019 Novel Coronavirus](#)

Outline

- ACES and ARBS
- NSAIDS
- Repurposed Drugs
- Remdesivir
- Convalescent SERA
- References

The severity and rapid spread of COVID-19 (caused by SARS-CoV-2) have raised questions about the use of some drugs in patients with the disease and whether currently available drugs could be effective in treating it. Definitive answers are lacking, but some recommendations can be made. Updated information on COVID-19 is available from the CDC at www.cdc.gov/coronavirus/2019-ncov/hcp/index.html.

ACES AND ARBS — Patients with cardiovascular disease are at increased risk of severe COVID-19. Some researchers have suggested that this increase in risk may be due to use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) in patients with diabetes, hypertension, or heart failure. The basis for this hypothesis is that ACE inhibitors and ARBs increase expression of ACE2 by epithelial cells in the lung, and pathogenic coronaviruses such as SARS-CoV-2 enter these cells via ACE2 receptors.¹ Others have suggested, however, that ACE2 may protect against lung injury in coronavirus infection and that taking an ACE inhibitor or an ARB might be beneficial.²

There is no clinical evidence to date that ACE inhibitors or ARBs increase or decrease the severity of COVID-19 and multiple medical organizations have advised against starting or stopping these drugs to prevent COVID-19 infection. Patients who are taking an ACE inhibitor or an ARB and subsequently develop COVID-19 should continue to take the drug.³

NSAIDs — The Health Minister of France has warned that use of nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen (*Advil*, *Motrin*, and others) to reduce fever in patients with COVID-19 increases the risk of severe adverse events and recommended use of acetaminophen (*Tylenol*, and others) instead.⁴ There is no convincing evidence that NSAIDs are especially dangerous for patients with COVID-19,⁵ but they can cause GI bleeding, fluid retention, and renal dysfunction in any patient, which can be dangerous for the critically ill. Controlled trials are lacking, but acetaminophen is an effective antipyretic and in recommended doses is less likely than an NSAID to cause serious adverse effects in most patients. Use of an NSAID or acetaminophen for continual fever suppression may reduce the immune response and prolong viral shedding. Patients who are taking NSAIDs for other indications should not stop taking them.

REPURPOSED DRUGS — In the absence of any FDA-approved drugs for treatment of COVID-19, many clinicians have turned to existing drugs to prevent or treat the disease. Some drugs that have been tried based on hypotheses or limited evidence include neuraminidase inhibitors used to treat influenza, HIV protease inhibitors, ribavirin, interferon, chloroquine/hydroxychloroquine, and azithromycin.⁶ Corticosteroids and interleukin-6 (IL-6) inhibitors have been used to suppress the inflammatory response. Evidence supporting off-label use of any of these drugs for treatment or prevention of COVID-19 is limited.

Neuraminidase inhibitors (e.g., oseltamivir) are not expected to be effective for prevention or treatment of COVID-19 because SARS-CoV-2 does not contain neuraminidase.

In a recently published clinical trial in 199 hospitalized patients with severe COVID-19 illness, addition of the HIV protease inhibitor combination **lopinavir/ritonavir** (*Kaletra*) to standard care was no more effective than standard care alone.⁷ Whether the combination might be effective in patients with less severe disease remains to be established. Lopinavir/ritonavir can cause GI adverse effects and QT interval prolongation,⁸ and it has the potential to interact adversely with many drugs.⁹ The Society of Critical Care Medicine recommends against the use of lopinavir/ritonavir in critically ill COVID-19 patients.¹⁰

In some US hospitals, **chloroquine and hydroxychloroquine** (*Plaquenil*, and generics) are being used off-label for treatment of patients with moderate or severe COVID-19 based on preliminary data from China and France showing that these drugs can reduce viral load and shorten the duration of symptoms. In one open-label study in 42 patients hospitalized for COVID-19 in France, addition of **azithromycin** (*Zithromax*, and generics) to hydroxychloroquine resulted in a more rapid decrease in viral load compared to treatment with hydroxychloroquine alone.¹¹ Clinical trials evaluating the efficacy and safety of these drugs for COVID-19 are in progress. These drugs can prolong the QT interval; interactions with other drugs, particularly those that also prolong the QT interval,⁸ are a concern with use of these drugs.

The CDC recommends that **corticosteroids** be avoided in most patients with COVID-19 because they may prolong viral replication; they are recommended for other indications such as asthma and for treatment of acute respiratory distress syndrome (ARDS) or refractory shock.^{10,12} Other immunomodulating drugs such as **IL-6 inhibitors** (e.g., tocilizumab [*Actemra*], sarilumab [*Kevzara*]) may mitigate the effects of cytokines released in response to the virus and limit lung damage in patients with severe disease; clinical trials are in progress.

Improper prescribing or stockpiling of repurposed drugs could result in toxicity and an inadequate supply for treatment of severe COVID-19 and other important indications, such as lupus and rheumatoid arthritis, and should be avoided. Until clinical trials establish the efficacy and safety of any drug for treatment of COVID-19, the CDC recommends supportive treatment and appropriate management of complications, such as ARDS and bacterial pneumonia.¹² Patients should be asked to participate in clinical trials of direct and supportive treatments.¹³

REMEDESIVIR — Remdesivir (Gilead), an investigational broad-spectrum IV antiviral drug that is active against SARS-CoV-2 and other coronaviruses *in vitro* and in animal models,¹⁴ is currently being studied in controlled trials in China and the US for treatment of severe COVID-19.

Gilead has temporarily stopped honoring requests for individual compassionate use of remdesivir, except for pregnant

women and children ≤ 18 years old with severe disease. Enrollment in clinical trials is recommended instead (<https://rdvcu.gilead.com>).

CONVALESCENT SERA — Until a vaccine becomes available, use of passive antibody therapy using the apheresed serum of recovered patients (no residual virus, high titers of neutralizing antibodies), which has been used in other viral epidemics, may be an option for prevention or early treatment of COVID-19. Limited data from the current COVID-19 outbreak in China suggest that use of convalescent sera reduced viral load and was safe. It might be especially beneficial for healthcare workers or family members of recently diagnosed patients.¹⁵ Studies in seriously ill patients will be conducted in the US.

REFERENCES

1. L Fang et al. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? *Lancet Respir Med* 2020 March 11 (epub).
2. MA Sparks et al. The coronavirus conundrum: ACE2 and hypertension edition. Available at: www.nephjc.com/news/covidace2. Accessed March 26, 2020.
3. ACC. HFSA/ACC/AHA statement addresses concerns re: using RAAS antagonists in COVID-19. Available at: <https://bit.ly/2UiMyt6>. Accessed March 26, 2020.
4. M Day. Covid-19: ibuprofen should not be used for managing symptoms, say doctors and scientists. *BMJ* 2020; 368:m1086.
5. FDA. FDA advises patients on use of non-steroidal anti-inflammatory drugs (NSAIDs) for COVID-19. Available at: <https://bit.ly/3dnggWX>. Accessed March 26, 2020.
6. C Harrison. Coronavirus puts drug repurposing on the fast track. Available at: www.nature.com/articles/d41587-020-00003-1. Accessed March 26, 2020.
7. B Cao et al. A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19. *N Engl J Med* 2020 March 18 (epub).
8. RL Woosley and KA Romero. QT drugs list. Available at www.crediblemeds.org. Accessed March 26, 2020.
9. Inhibitors and inducers of CYP enzymes and P-glycoprotein. *Med Lett Drugs Ther* 2019 November 6 (epub). Available at: medcalletter.org/downloads/CYP_PGP_Tables.pdf.
10. W Alhazzani et al. Surviving sepsis campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). Available at: <https://bit.ly/33KvsJj>. Accessed March 26, 2020.
11. P Gautret et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents* 2020 March 17 (in press).
12. CDC. Interim clinical guidance for management of patients with confirmed coronavirus disease (COVID-19). Available at: <https://bit.ly/2Qy1qTH>. Accessed March 26, 2020.
13. S Murthy et al. Care for critically ill patients with COVID-19. *JAMA* 2020 March 11 (epub).
14. ML Agostini et al. Coronavirus susceptibility to the antiviral remdesivir (GS-5734) is mediated by the viral polymerase and the proofreading exoribonuclease. *mBio* 2018; 9:e00221.
15. A Casadevall and LA Pirofski. The convalescent sera option for containing COVID-19. *J Clin Invest* 2020 March 13 (epub).

Two Drugs for Sickle Cell Disease: Crizanlizumab (Adakveo) and Voxelotor (Oxbryta)

Med Lett Drugs Ther. 2020 Apr 6;62(1595):51-2

Summary: Crizanlizumab (Adakveo) and Voxelotor (Oxbryta)

- IV crizanlizumab blocks adhesion of platelets,

Outline

- Standard Treatment