UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

PALLIATIVE CARE PHARMACY PHAST PHACT

March 19th, 2020 **Vol. 6, No. 11**

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If you have a topic you would like the pharmacy team to answer, please send your suggestions to: pruskowskija@upmc.edu

SPECIAL EDITION:

Pharmacological Options for COVID-19

Background:

Coronoviruses are a group of related viruses that can cause disease in mammals and birds. Rarely, animal coronaviruses can emerge to infect humans. This was expected to occur during the Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). In humans, coronaviruses can cause respiratory tract infections that can vary from mild common cold symptoms, to severe respiratory failure. From what we currently know, COVID-19 ("corona" + "virus" + "disease" of 2019), first detected in Wuhan (Hubei Province within the People's Republic of China), is a positive-sense single-stranded RNA virus that is transmitted primarily via respiratory droplets within a range of 6 feet. Indirect contact via contaminated surfaces is another possible cause of infection.

Importance:

On March 13th, 2020, the United States Government declared a National Emergency due to COVID-19. This novel disease has cause rapid and worldwide spread which has triggered unprecedented social distancing measures. Early information has indicated older adults, and those with serious medical conditions (such as heart disease, diabetes and lung disease), are at highest risk of experiencing serious forms of infection. Palliative care providers often care for these patients. In addition to other CDC Guidance, palliative care providers should be aware of pharmacological options for COVID-19.

The Literature:

- Drug Discov Ther. 2020;14(1):58–60.
  Discovering drugs to treat coronavirus disease 2019 (COVID-19).

- Several drugs such as chloroquine, arbidol, remdesivir, and favipiravir are currently undergoing clinical studies to test their efficacy and safety in the treatment of coronavirus disease 2019 (COVID-19) in China; some promising results have been achieved thus far. This article summarizes agents with potential efficacy against SARS-CoV-2.
- "There are no finally verified antivirals specific to COVID-19 at present. The efficacy and safety of these candidate drugs in the treatment of COVID-19 need to be confirmed in further preclinical and clinical trials."
- Table 1. Antiviral included in the Guidelines (version 6) for the treatment of COVID-19

Drug	Dosage	Method of administration	Duratio
IFN-α	5 million U or equivalent dose each time, 2 times/day	Vapor inhalation	No mor
Lopinavir/ritonavir	200 mg/50 mg/capsule, 2 capsules each time, 2 times/day	Oral	No mor
Ribavirin	500 mg each time, 2 to 3 times/day in combination with IFN-α or lopinavir/ritonavir	Intravenous infusion	No mor
Chloroquine phosphate	500 mg (300 mg for chloroquine) each time, 2 times/day	Oral	No mor
Arbidol	200 mg each time, 3 times/day	Oral	No mor

- Biosci Trends. 2020;14(1):72–73.

Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies.

- Chloroquine phosphate, an old drug for treatment of malaria, is shown to have apparent efficacy and acceptable safety against COVID-19 associated pneumonia in multicenter clinical trials conducted in China. The drug is recommended to be included in the next version of the Guidelines for the Prevention, Diagnosis, and Treatment of Pneumonia Caused by COVID-19 issued by the National Health Commission of the People's Republic of China for treatment of COVID-19 infection in larger populations in the future.

- mBio. 2018;9(2):e00221-18.

Coronavirus Susceptibility to the Antiviral Remdesivir (GS-5734) Is Mediated by the Viral Polymerase and the Proofreading Exoribonuclease.

- Coronaviruses (CoVs) cause severe human infections, but there are no approved antivirals to treat these infections. Development of nucleoside-based therapeutics for CoV infections has been hampered by the presence of a proofreading exoribonuclease. Here, we expand the known efficacy of the nucleotide prodrug remdesivir (GS-5734) to include a group β-2a CoV. Further, GS-5734 potently inhibits CoVs with intact proofreading. Following selection with the GS-5734 parent nucleoside, 2 amino acid substitutions in the nsp12 polymerase at residues that are identical across CoVs provide low-level resistance to GS-5734. The resistance mutations decrease viral fitness of MHV *in vitro* and attenuate pathogenesis in a SARS-CoV animal model of infection. Together, these studies define the target of GS-5734 activity and demonstrate that resistance is difficult to select, only partial, and impairs fitness and virulence of MHV and SARS-CoV, supporting further development of GS-5734 as a potential effective pan-CoV antiviral.

So… What does this all mean Jenn?

- While there are no verified agents, several novel antiviral agents have been explored for the treatment of coronaviruses including COVID-19
- Preliminary trials suggest chloroquine (hydroxychloroquine) or remdesivir (via a clinical trial or compassionate use) may be reasonable options for patients with a confirmed case of COVID-19
- Hydroxychloroquine is already FDA approved. It is usually dosed 200-800mg in daily divided doses and it does not require renal or hepatic adjustment. Most common adverse reactions include: retinopathy, ataxia, dizziness, headache, nausea/vomiting, mood changes, skin rash or itching, or hair loss. Hydroxychloroquine is also relatively inexpensive (approximately $2-4/tablet)
- Remdesivir is RNA synthesis inhibitor, and is currently an investigational agent within the US. Initial trials have been limited to patients >/= 18 years of age, and is dosed 200mg one day 1, followed by 100mg once daily for a duration of 5-10 days
- Take a look at the UPMC stance on potential treatments for COVID-19 and work with your individual inpatient pharmacy for more information regarding available agents for patients with confirmed COVID-19 cases

CLINICAL PEARL:
Currently, it is reasonable to consider hydroxychloroquine or remdesivir (via clinical trial or compassionate use) for confirmed COVID-19 cases.