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I have been a practicing Rheumatologists for 30 years. I was trained at New York University and Albany Medical Center. In Rheumatology, we treat patients with over-reactive immune system resulting/causing serious autoimmune diseases. The goal is to treat to target using combination therapy with different modes of action to complement each medication.

Physicians around the world have been working hard to treat Covid-19 patients. However, the results are not satisfactory for the seriously ill. I believe that medications are being given **too late in the disease process**.

I am proposing:

"One-Step Ahead" Treatment Plan

- 1. Using antioxidant, such as N-acetylcysteine (NAC) which is available at low cost without prescription, 1000 mg twice a day, as a preventative **pretreatment to boost the immune system**. During viral infection, oxidative stress is partially responsible for pulmonary damage, causing organ failure and acute respiratory distress syndrome (ARDS).
- 2. Once a patient is symptomatic with mild disease of fever and/or mild/moderate cough, (e.g., days 1 to 7), then add Hydroxychloroquine 200 mg twice a day for 10 days. Oseltamivir should also be added if influenza testing is positive.
- 3. With the onset of shortness of breath, moderate disease activity, usually around day 7, oral Lopinavir/Ritonavir 200mg/50mg two tablets twice a day should be added to the antioxidant, **as an outpatient**. Please note: avoid the combination of Lopinavir/Ritonavir with Hydroxychloroquine, which may cause serious arrhythmia and drug interactions due to an increased QT interval.
- 4. For patients with moderate to severe elevated CRP and mild pneumonia, (usually between days 7 and 15) IL-6 inhibitors, e.g, Tocilizumab or Sarilumab sub Q injections, may be considered **as an outpatient**, before the onset of ARDS and sepsis. Since cytokines and chemokines produced as part of host response to the infection contribute to the pathogenesis of tissue damage.
- 5. **Once a patient is hospitalized**, consider **early use of** Remdesivir IV, Tocilizumab IV or Sarilumab IV, before the need of intubation, onset of sepsis or ARDS.

In summary, NAC should be used for preventative treatment to boost immune system and add antivirals/anti-inflammatory treatment early before the onset of sepsis or ARDS.

Based on an extensive research, I originally formulated this strategy for my family and my patients, in the unfortunate event that they become infected. While this is NOT an FDA approved treatment, time is the essence in a pandemic situation. I hereby humbly encourage my physician colleagues to consider its use for improved clinical outcomes and decreased need of hospitalization, ICU and intubation.

Key References:

Clinical Characteristics of Coronavirus Disease 2019 in China, *New England Journal of Medicine*, February 28, 2020

Kwak Sung Sun, Physicians Workout Treatment Guidelines for Coronavirus. *Korea Biomedical Review*, Updated Feb 13, 2020

Katia Aquilano et al, Glutathione: New Role in Redox Signaling for an Old Antioxidant. *Frontiers in the Pharmacology*, 26 August 2014