Treatment Algorithm for COVID-19

SARS-CoV-2 (aka COVID-19) positive or strongly suspected Is patient presently hospitalized or requires inpatient management? No Yes Consider antibiotics for secondary bacterial pneumonia if concerned · Stay home and avoid close contact Avoid corticosteroids unless indicated for separate process with others to minimize spread • Drink plenty of water (e.g., septic shock, COPD, asthma, ARDS etc.) · Symptomatic care for fever, cough, congestion, pain • Avoid corticosteroids unless re-Patient has any of the following AND confirmed SARS-CoV-2? quired for other condition (e.g. Age ≥ 65 years COPD exacerbation) Significant history of lung and/or heart disease • If shortness of breath develops, History of transplantation (solid organ or hematologic) seek immediate medical evaluation Other immunocompromising condition and/or receiving immunosuppressive medications Moderate to severe infection: Radiographic evidence of pneumonia requiring supplemental oxygen and/or mechanical ventilation Yes No **Supportive Care Measures Clinical Status** Evidence of hyperinflammatory Worsening oxygen requirements, mechanical Stable supplemental ventilation or expected need for ventilation response oxygen requirements (Criteria Page 2) within 48 hrs, or immunocompromised? Antiviral therapy may be considered* Consideration of IL-6 Inhibition **Please contact ID and/or Antimicrobial Stewardship with questions, or (In accordance with system or if planning to start empirically while COVID-19 test still pending** clinical trial criteria on Page 2) First-line: Hydroxychloroquine⁵⁻⁷ 400mg PO BID for one day, then 200mg PO BID x 4 days (total duration = 5 days)

Sarilumab

Clinical Trial (Anschutz Only) Tocilizumab (All UCHealth)

• Monitor for visual changes, neuropathy, QTc prolongation, and cytopenias <u>Second-line</u>: Lopinavir/ritonavir (LPV/r) ^{1-4, 8} 400mg/100mg PO BID ± Ribavirin (dosing on Page 2) x 5 days

Pregnancy category C, human data in malaria does not show increased risk

- LPV/r pregnancy category C, human data does not show increased teratogenic risk
- Ribavirin pregnancy category X

Caution in liver disease

Low drug interaction potential

- Significant drug interaction potential with LPV/r (Overview Page 3-6)
- Monitor for QTc prolongation, liver impairment, cytopenias, and diarrhea
- PO ribavirin preferred
- Inhaled ribavirin discouraged, consideration with ID and ID pharmacy

Third-line: Nitazoxanide⁶ 1,000mg PO BID x 5 days

*Agents are not approved for CoV infections, and limited evidence supports possible benefit in COVID-19 infection, weigh risks and benefits prior to initiation. Data is rapidly evolving with therapeutics for COVID-19 and recommendations are subject to change rapidly. Please refrain from printing this document.

Oral Ribavirin Dosing for Treatment of COVID-19

- CrCl > 50: Load 10 mg/kg (max 2 gram) PO x 1, then 400 mg (40-60kg), 600 mg (61-90kg), 800 mg (91-120kg), or 1000 mg (> 120 kg) PO TID.
- CrCl 30-50: Load 10 mg/kg (max 2 gram) PO x1, then 200mg PO TID
- CrCl < 30/HD: Load 10 mg/kg (max 2 gram) PO x1 , then 200mg PO daily (limited data)

 For lung transplant, omit loading dose and start 15-20mg/kg/day in 3 divided doses; Round all doses to nearest 200 mg

In Depth Drug Interactions Website: http://www.covid19-druginteractions.org/

System Criteria for Tocilizumab Use

- Confirmed COVID-19 positive
- Critical illness associated with COVID-19 evidenced by:
 - Respiratory failure requiring mechanical ventilation or
 - Shock or
 - Combined failure of other organs requiring ICU care
- Evidence of ≥2 abnormalities associated with hyperinflammatory response/cytokine release:
 - D-Dimer > 1 mcg/mL
 - Serum ferritin > 600 mcg/L
 - Persistent fever > 38.3°C
 - C-Reactive Protein > 100 mg/L
 - Interleukin-6 ≥ 3x ULN
- Ordered/recommended by Infectious Diseases or Pulmonology Services
- Review and approval by secondary provider(s) not directly involved in the patients care
- ALT/AST < 5x ULN
- Platelet Count is ≥ 50.000/mm3
- Absolute Neutrophil Count (ANC) is ≥ 500/mm3
- No presence of active or strongly suspected bacterial or fungal infection. Stability of these infections with appropriate antibiotics/antifungals and proceeding with tocilizumab should be carefully weighed by ordering/consulting infectious diseases and/or pulmonology physician.

Sarilumab Clinical Trial Criteria

References:

- 1. Chu CM, et al. Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. Thorax. 2004; 59: 252-6.
- 2. Chan KS, et al. Treatment of severe acute respiratory syndrome with lopinavir/ritonavir: a multicentre retrospective matched cohort study. *Hong Kong Med J.* 2003; 9: 399-406.
- 3. Park SY, et al. Post-exposure prophylaxis for Middle East respiratory syndrome in healthcare workers. J Hosp Infect. 2019; 101(1): 42-6.
- 4. Young BE, et al. Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore. JAMA. 2020; epub
- 5. Gao J, et al. Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. *Biosci Trends*. 2020: ebup.
- 6. Wang M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Research. 2020; 30: 269-71.
- 7. Gautret et al. (2020) Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. International Journal of Antimicrobial Agents In Press 17 March 2020 DOI: 10.1016/j.ijantimicag.2020.105949
- 8. Cao B, et al. A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19. N Eng J Med. 2020; epub—DOI: 10.1056/NEJMoa2001282