1. Recommended treatments/therapies
   1. Antibacterials for co-infection
      1. CTX + doxy/azithro
      2. Cefepime + doxy/azithro +/- vanc (+MRSA nasal swab)
   2. COVID-19 directed therapy 1-5, hydroxychloroquine utilization restricted to Infectious Diseases, Critical Care, and Pulmonology:

|  |  |  |  |
| --- | --- | --- | --- |
| Severity | Criteria | Treatment | Notes |
| Mild | Not requiring hospitalization  OR  Hospitalized with SpO2 > 94% and NO radiographic evidence of pneumonia | Supportive Care |  |
| Moderate | Hospitalized with SpO2 < 94%  AND  Radiographic evidence of pneumonia | Hydroxychloroquine 400mg PO q12h x 2 doses  THEN  Hydroxychloroquine 200mg PO q12h x 8 doses | -Check EKG prior to hydroxychloroquine initiation for QT prolongation  -Review potential medication interactions and other possible side effects |
| Severe with respiratory failure (*no other end organ damage)* | Patient requiring mechanical ventilation  AND   1. Not on pressors 2. CrCl > 30ml/min 3. ALT < 5x ULN | Hydroxychloroquine 400mg PO q12h x 2 doses  THEN  Hydroxychloroquine 200mg PO q12h x 8 doses  Initiate remdesivir compassionate use pathway (<https://rdvcu.gilead.com/>) | -Check EKG prior to hydroxychloroquine initiation for QT prolongation.  -Review potential medication interactions and other possible side effects (below)  -Remdesivir is NOT to be used concomitantly with hydroxychloroquine or other antivirals |
| Severe with respiratory failure (*+ evidence of other end organ damage)* | Patient requiring mechanical ventilation  AND   1. Requiring pressors 2. CrCl < 30ml/min, RRT 3. ALT > 5x ULN | Hydroxychloroquine 400mg PO q12h x 2 doses  THEN  Hydroxychloroquine 200mg PO q12h x 8 doses | -Check EKG prior to hydroxychloroquine initiation for QT prolongation  -Review potential medication interactions and other possible side effects (below)  -Not candidate for remdesivir compassionate use |

1. Comment regarding ACE inhibitors/ARBS, NSAIDs 6-8
   1. As previously shown for SARS-CoV, COVID-19 similarly utilizes angiotensin-converting enzyme-2 (ACE2) as a receptor for viral cell entry
   2. ACE2 expression is up-regulated by these medications
      1. Theoretical risk of facilitation of viral entry into ACE2 presenting cells
      2. At this time no clinical evidence that taking ACEi, ARB, or ibuprofen increase risk of acquiring COVID-19 or increase disease severity
      3. The World Health Organization has retracted it’s advisory to avoid ibuprofen in COVID-19 patients (3.18.2020)
   3. **Not enough information to recommend discontinuation of ACEi or ARB to mitigate risk of COVID-19**
2. Controversial/investigational Agent not routinely recommended. This list is not exhaustive of all agents:

|  |  |
| --- | --- |
| **Agent/Class** | **Comment** |
| Corticosteroids  (Inhaled and Systemic) | Use is situational. Not recommended in early or mild disease. Consider in critical cases with ARDS and cardiac involvement. |
| Hydroxychloroquine + Azithromycin | Current data insufficient to establish efficacy of this combination in the treatment of COVID-19.9 Both medications carry risk of QT prolongation and potentially fatal arrhythmia. |
| Lopinavir/Ritonavir | No significant differences in reduction of viral RNA load, duration of viral RNA detectability, duration of oxygen therapy, duration of hospitalization, or time from randomization to death vs standard of care.10 |
| Influenza treatments  (Oseltamivir, Zanamivir, Baloxavir) | No data to support use in the treatment of COVID-19. Neither oseltamivir nor zanamivir has demonstrated inhibition of cytopathic effect of SARS-CoV in *in vitro* cell culture.11 Additionally coronaviruses do not utilize neuraminidase for the budding stage of reproduction. |
| IVIG | No data to support use in the treatment of COVID-19. Remains on shortage nationwide. Clinical trial planned, not yet enrolling (NCT04261426). |
| Convalescent Plasma | No data to support use in the treatment of COVID-19. Safety and efficacy have not been established in the treatment of COVID-19 and no protocols have been established for use. |
| Nafamostat | No data to support use in the treatment of COVID-19. Inhibits MERS but use for COVID-19 is unknown. 3 |
| Anti-IL6 monoclonal antibodies  (Tocilizumab, Sarilumab) | No data to support use in the treatment of COVID-19. In China, tocilizumab can be used to treat severely or critically ill COVID-19 patients with extensive lung lesions and high IL-6 levels. Adverse effects can be severe and long-lasting; risk of secondary infection is possible and unquantified. |
| Indomethicin | No data to support use in the treatment of COVID-19. One in vitro & animal model study with other coronaviruses, SARS-CoV & CanineCoV.12 |
| Vitamin C | No data to support use in the treatment of COVID-19. There is an ongoing clinical trial of high-dose vitamin C for treatment of COVID-19 in China (NCT04264533), currently recruiting. |
| Nitazoxanide | No data to support use in the treatment of COVID-19. Some *in vitro* evidence to suggest effect. 3 |

References:

1. Biosci Trends. 2020; 14(1):72-73.
2. Clin Infect Dis 2020 (epub ahead of print) doi: 10.1093/cid/ciaa237
3. Cell Res 2020;30: 269–271
4. Int J Antimicrob Agents 2020 (epub ahead of print) doi: 10.1016/j.ijantimicag.2020.105932
5. Antimicrob Agents Chemother 2020 (epub ahead of print) doi: 10.1128/AAC.00399-20
6. Lancet Respir Med 2020 (epub ahead of print) doi: 10.1016/S2213-2600(20)30116-8
7. Eur Heart J 2020 (epub ahead of print) doi: 10.1093/eurheartj/ehaa235
8. HFSA/ACC/AHA Statement Addresses Concerns Re: Using RAAS Antagonists in COVID-19. (<https://www.acc.org/latest-in-cardiology/articles/2020/03/17/08/59/hfsa-acc-aha-statement-addresses-concerns-re-using-raas-antagonists-in-covid-19>). Accessed 3.20.20.
9. Int J Antimicrob Agents 2020 (epub ahead of print). doi: 10.1016/jantimicag.2020.105949
10. N Engl J Med 2020 (epub ahead of print). doi: 10.1056/NEJMoa2001282
11. Emerg Infect Dis 2004;10(4): 581–6.
12. Antivir Ther 2006;11(8):1021-30.