



**Hydroxychloroquine**

- 400mg PO/NG tube BID x 1 day, then 200mg PO/NG tube BID x 4 days

OR

**Chloroquine (if hydroxychloroquine is unavailable)**

- 500mg PO/NG tube BID x 10 days

AND

**ZINC Sulfate (Consider adding Vit C/D)**

- 220 mg PO daily x 5 days

± **Azithromycin\***

- 500mg PO/NG tube x 1, then 250mg PO/NG tube daily x 4 days

\*Cardiac monitoring for QTc prolongation is required for patients on hydroxychloroquine or chloroquine with azithromycin. Order baseline EKG, and monitor QT interval daily while on therapy.

**NOTE: Therapeutic options are OFF-Label at this time. Recommendations subject to change based on product availability & further clinical trial evidence. Infectious Disease, Pulmonologist, & Intensivist restrictions apply.**

**Discontinue Therapy**

• **Tocilizumab (Actemra)** 400 mg IV x 1 dose. May repeat x 1 in 12 hours if needed (max of 800mg)

OR

• **Sarilumab (Kevzara)** 200mg SubQ x 1 dose; no repeat

**Monitor and Continue Same Therapy**

### Suggested approach to prophylaxis of COVID-19:

- While there is very limited data (and none specific for COVID-19), the following “cocktail” may have a role in the prevention/mitigation of COVID-19 disease, especially amongst those with medical comorbidities.
- While there is no high-level evidence that this cocktail is effective; it is cheap, safe and should be readily available.

### Anticoagulation:

- Elevated d-dimer levels (> 1 mg/dL) has been shown to have increased odds of in-hospital death.
- ALL patients should receive routine VTE prophylaxis, unless otherwise contraindication (& documented).
- Strongly consider adjusting full anticoagulation therapy if d-dimer levels elevated (i.e. 1-5 mg/dL).
- Full therapy (LMWH preferred):
  - Enoxaparin SubQ 1 mg/kg subQ Q 12Hr
  - AKI/ESRD/anuric - start low-intensity heparin infusion (No bolus required, if no confirmed VTE).
- Renal dose adjustments apply.
- Consider further dose adjustments if fibrinogen is low.

### Other Therapies (currently lacking evidence):

1. **Baloxavir (Xofluza)**
2. **Inhaled Nitric Oxide**
3. **Nicolosamide**
4. **Oseltamivir (Tamiflu)**
5. **Sirolimus (Rapamune)**

*No Evidence of Harm or Benefit:*

6. **ACE Inhibitors and ARBS**
7. **NSAIDS** – speculation based on up regulation of ACE2 receptors.

### Alternative Therapies (pending further data/evidence):

1. **Convalescent Plasma** – studied in various outbreaks, but not yet been shown to be effective in COVID-19.
  - Investigational agent available via expanded access trial. Mayo Clinic Protocol (NCT04325672).
  - Treatment Strategy: 1-2 units (300-600ml) plasma with at least a 1:64 titer of anti-SARS-CoV-2.
  - Inclusion criteria:
    - Hospitalized patients  $\geq$  18 yrs.
    - Confirmation of SARS-Cov-2 by PCR
  - Exclusion criteria:
    - Females who are pregnant or breastfeeding
    - Patient received IVIG in past 30 days
    - Any contraindication to transfusion
2. **Lopinavir and Ritonavir (Kaletra)** – time to clinical improvement was not shorter than with standard care.
  - Medication has no impact on viral load.
  - Efficacy for treatment of COVID-19 not definitely established.
  - Consider in patients who are pregnant or breastfeeding.
3. **Remdesivir**
  - Investigational drug and not commercially available. (*Expanded access clinical trial program pending*)
  - Safety and efficacy not established.
  - Inclusion criteria:
    - ICU admission
    - Confirmation of SARS-Cov-2 by PCR
    - On mechanical ventilation
  - Exclusion criteria:
    - Multiorgan failure
    - Pressor requirement to maintain blood pressure
    - CrCl <3 0 ml/min or on dialysis
    - ALT level > 5x upper limit
    - Cannot be used in conjunction with other experimental antiviral agents for COVID-19
  - ADEs: LFT abnormalities, reversible kidney injury, hypotension during infusion
4. **Supplements**
  - Vitamin C 500 mg BID and Quercetin 250-500 mg BID.
  - Melatonin (slow release): Begin with 0.3mg and increase as tolerated to 1-2 mg at night.
  - Vitamin D3 1000-4000 u/day. Most likely benefit in patients with low baseline 25- OH vitamin D levels and those living at over 40° latitude.

### Adjunct Therapies (conflicting/LITTLE to NO data):

1. **Corticosteroids** – conflicting studies
  - Hydrocortisone 50 mg Q6Hrs for 7 days or methylprednisolone 60 mg IV daily for 7 days.
  - Methylprednisolone – appeared to reduce the risk of death in confirmed COVID-19 pneumonia patients who developed ARDS.
  - BOTH corticosteroids AND vitamin C are required to down-regulate the cytokine storm.
  - Evidence suggests that corticosteroids in patients with SARS and MERS showed no survival benefit and possible harm.
  - WHO and CDC recommend not to be routinely used in pts with COVID-19 for treatment of viral pneumonia or ARDS unless indicated for another reasons (i.e. asthma, COPD exacerbation, septic shock).
2. **Statin therapy**
  - Atorvastatin 40-80 mg/day.
  - May reduce mortality in the hyper-inflammatory ARDS phenotype.
  - Pleotropic anti-inflammatory, immunomodulatory, antibacterial and antiviral effects.
  - Decreases expression of PAI-1.

### Precautions or Contraindications (CI):

1. **Hydroxychloroquine and Chloroquine**
  - Risk for QTc prolongation (>500 msec).
  - Discontinue all other non-essential QTc prolonging medications.
  - Risk of hemolysis, suggest baseline G6PD test.
  - Separate by at least 4 hours if taking antacids.
  - ADEs: hypoglycemia, bone marrow suppression, cardiac arrhythmia.
2. **Azithromycin**
  - Absolute CI: macrolide hypersensitivity, jaundice, hepatitis.
  - Increased risk of QTc prolongation.
3. **Tocilizumab (Actemra) and Sarilumab (Kevzara)**
  - Black Box Warning: increased risk of infection
  - ADEs: LFT abnormalities, myelosuppression, worsening or unmasking of infection; which may be severe, headache, hypertension, injection site reactions, GI perforation.

## GENERAL SCHEMA FOR RESPIRATORY SUPPORT IN PATIENTS WITH COVID-19

(Try to avoid intubation if possible)

