University Hospital of Brooklyn Guidance Document for COVID-19 (SARS-CoV-2) Treatment†

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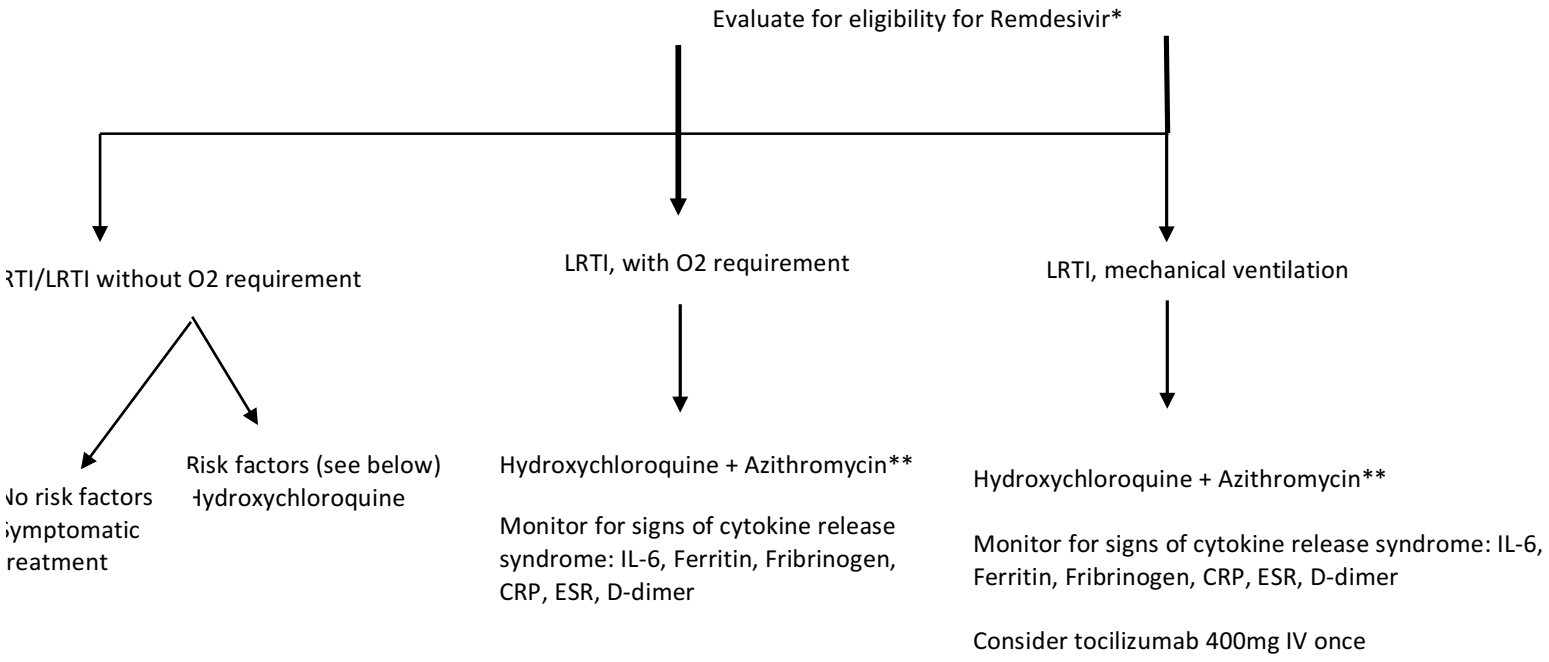
This document suggests guidance for the use of anti-infectives to treat patients at UHB with confirmed or highly suspected SARS-CoV-2 infection. It makes use of whatever evolving data and community practice exist. The interventions below are not supported by significant trials and are being suggested for use assuming a risk versus benefit analysis. Clinicians are not required to follow these suggestions. Whenever possible clinicians should engage in discussions with patients and their families for whom these therapies are being considered.

In a patient with **positive SARS-CoV-2 PCR test** or **highly suspected person under investigation** for COVID-19 (contact with a confirmed case or high-risk travel history or clinical presentation)

1. Baseline evaluation
    a) CBC, CMP, serum ferritin, CRP, influenza/rsv PCR, EKG, blood cultures x2 sets, procalcitonin, HIV, pregnancy test (if applicable), chest x-ray
2. Consider COVID -19 **TREATMENT** for the following **GROUPS:**
    a) Requiring ICU-level of care (see below on additional treatment consideration)
    b) Requiring any supplemental oxygen (if not on oxygen at baseline)
    c) Lower respiratory tract disease with risk factors for progression to severe disease:
        1. Age > 60 years
        2. Immunocompromised (includes: chemotherapy, steroids >/= 20mg QD, hematologic malignancies, advanced HIV disease (detectable HIV VL or CD4 count<200 cells/mm3, HCW/first responder with known/probable aerosol exposure, on immunosuppressive therapy)
        3. Significant chronic comorbidities (including but not limited to diabetes, pulmonary disease [e.g. COPD], cirrhosis, CKD, coronary heart disease, hypertension, and any other medical conditions based on clinical judgement by Infectious Disease Attending

Algorithm for management of patients with COVID-19



URTI: Upper respiratory tract infection, defined as sore throat, URI symptoms, with LRTI symptoms.

LRTI: Lower respiratory tract infection, defined as cough, shortness, of breath, hypoxemia, or radiographic changes on CXR.

*Information for compassionate use (https://rdvcu.gilead.com). Exclusion: multi-organ failure, pressor requirement, ALT levels > 5 X ULN, continuous veno-venous hemofiltration CrCl<30

mL/min

3. Treatment recommendations qualifying groups per treatment indications as above:

   a) Supportive care as usual by primary team
   b) Treat with **hydroxychloroquine (HCQ). Needs ID approval.**
      - Use for patients with documented SARS-CoV2
      - Consider for patients with mild to moderate disease and risk factors not requiring supplemental oxygen
      - Use as primary treatment if not a candidate for remdesivir compassionate use (see 2d below) or in the interim pending receipt of remdesivir for compassionate use
      - Dose: 400 mg BID x 1 day, then 200 mg BID for at least 4 more days (extend duration depending on clinical response) BID (total duration at least 5 days, not exceeding 10 days)
      - Can be compounded in a suspension. No adjustment for renal or hepatic dysfunction.
      - Add Azithromcyin 500mg orally or IV once then 250mg daily for four days in patients who require ICU care/supplemental oxygen/mechanical ventilation
      - **Assess risk for QT prolongation-check baseline EKG: if QTc>500ms would avoid. Otherwise check rhythm strip/QTc 2-3 hr after dose- if no change continue. If QTc >550ms but <600ms eliminate azithromycin. If QTc>600 stop both drugs. Most important assessment is the baseline QTc!)
   c) Attempt to obtain **remdesivir** via **compassionate use** through Gilead (http://rdvcu.gilead.com/)

      - Inclusion criteria: hospitalization | confirmed SARS-CoV-2 by PCR | **mechanical ventilation**
      - Exclusion criteria: multiorgan failure | requiring pressors | ALT >5x ULN | CrCl <30 or any dialysis
      - May need to **discontinue** hydroxychloroquine (or alternative) prior to start of remdesivir (follow Gilead's compassionate use protocol for remdesivir for definitive instructions)

   d) Additionally, for patients requiring ICU-level of care for COVID-19-related severe pulmonary complications – in addition to the treatments listed above, consider use of IL-6 receptor antagonist (estimated cost ~$2,500-6,000 per dose)
      - **Tocilizumab** (Actemra). **Needs ID approval**.
        - 400 mg IV, one time
          - OR

        - <30 kg: 12 mg/kg
        - ≥30 kg: 8 mg/kg (maximum dose: 800 mg per dose IV)
            - If clinical improvement does not occur after the first dose, up to 3 additional doses may be administered (with at least an 8 hour interval between consecutive doses)
        - Warnings/adverse effects
            - Perforated diverticulitis
            - Neutropenia/thrombocytopenia
            - Hepatotoxicity
            - Zoster reactivation
            - Infections (bacterial, fungal, viral, protozoal, TB and other opportunistic infections)
            - Worsening demyelinating CNS disease
            - Consider sending out IL-6 plasma level (https://www.mayocliniclabs.com/test-catalog/Overview/63020)
                - Send out test, won't likely influence real-time decision-making but potentially useful for further understanding of pathogenesis of severe COVID-19

e) Contraindications
    - Hydroxychloroquine
        - Known hypersensitivity to hydroxychloroquine
        - Marked QTc prolongation (avoid concomitant azithromycin or fluoroquinolones)
        -

f) Monitoring
    - Hydroxychloroquine
        - EKG monitoring if QTc elevated, or if concomitant therapy with medications that can prolong QTc
        - Periodic CBC and CMP
        - If on anti-diabetic medications or symptoms of hypoglycemia, monitor fingersticks
    - Tocilizumab
        - Periodic CBC, CMP

Additional points:

- **Corticosteroids** – have no effect on mortality and may result in delayed viral clearance [Huang et al]. NOT recommended by CDC, unless indicated for other evidence-based reasons (e.g. COPD exacerbation or septic shock) per those guidelines [CDC].
- **ACE inhibitors/ARBs** – there is a working HYPOTHESIS (no clinical or experimental data at this time) that patients on these drugs maybe at increased risk for developing severe disease [Fang et al]
    - SARS-CoV-2 binds to ACE2, expressed by epithelial cells of lung, intestine, kidney and blood vessels

- Expression of ACE2 is increased/upregulated in patients with DM and hypertension, who are treated with ACE inhibitors or ARBs. ACE2 is also increased by TZDs and ibuprofen.
- Increased expression of ACE2, in theory, would facilitate infection with COVID-19
- In theory, patients with cardiac diseases, hypertension, or diabetes, who are treated with ACE2-increasing drugs, are at higher risk for severe COVID-19 infection – no evidence CCBs increase ACE2 expression so [Fang et al] raise CCBs can be potential alternative. This is not validated by any data.
- The Council on Hypertension of the European Society of Cardiology strongly recommend that physicians and patients should continue treatment with their usual anti-hypertensive therapy because there is no clinical or scientific evidence to suggest that treatment with ACEi or ARBs should be discontinued because of the Covid-19 infection.

† This guidance document is based on little currently available data and is subject to change. These suggestions for therapy are not meant to serve as a 'guideline' and clinicians must consider many factors before initiating any treatment for COVID19.

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