BRIGHAM HEALTH
BRIGHAM AND WOMEN'S HOSPITAL

Last Updated March 18, 2020

Brigham & Women's Hospital Inpatient COVID-19 Treatment Guidelines

There are no FDA-approved therapeutics for COVID-19**. The following guidance is based on available pre-clinical and limited clinical evidence regarding investigational treatments that may have efficacy against Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV)-2 or in mitigating a deleterious host immune response to COVID-19 disease. **Infectious disease consult** is recommended in patients who are being considered for COVID-19 treatment. This guidance document will be updated frequently to include new or emerging data and is **for inpatient use only**

Type of Patient	Clinical Presentation	Treatment	Ongoing Clinical Trials
Prevention or post-exposure prophylaxis	N/A	Not recommended at this time given lack of data and limited supplies of investigational agents	
Asymptomatic	N/A	Not recommended at this time given lack of data and limited supplies of investigational agents	
Patients with mild respiratory symptoms, but no risk factors for progression to severe disease[1]	May include fever (>37.2°C), sore throat, cough, and/or myalgias; no dyspnea	Supportive care, treatment not recommended	
Patients with mild respiratory symptoms plus ≥1 risk factor for progression to severe disease[1]	May include fever, sore throat, cough, and/or myalgias; no dyspnea	Consider hydroxychloroquine	
Patients with moderate COVID-19 disease	May include fever, dyspnea, and/or chest imaging consistent with COVID-19 pneumonia	Consider remdesivir via open-label clinical trial for moderate disease (SpO2 >94% on room air) • If remdesivir is not available, consider hydroxychloroquine	Remdesivir Trial: NCT04292730 PI: Francisco Marty (p37491)
Patients with severe COVID-19 disease	May include fever, dyspnea, and/or chest imaging consistent with COVID-19 pneumonia requiring supplemental oxygen	Consider remdesivir via open-label clinical trial for severe disease (SpO2 ≤94% on room air) • If remdesivir is not available, hydroxychloroquine may be used Consider tocilizumab (see page 3 for specific criteria for use)	Remdesivir Trial: NCT04292899 PI: Francisco Marty (p37491)
Patients critically ill with severe COVID-19 disease	Respiratory failure, acute respiratory distress syndrome (ARDS), systemic inflammatory response syndrome (SIRS), multi-organ failure	Consider hydroxychloroquine until remdesivir trial is potentially opened for this population Consider tocilizumab (see page 3 for specific criteria for use)	

[1] Risk factors for progression to severe disease include age >60 years, immunocompromising conditions, active malignancy, structural lung disease, chronic kidney disease, hypertension, coronary artery disease, or diabetes in patients requiring admission for treatment of COVID-19 disease

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COVID-19 Investigational Therapies

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Hydroxychloroquine (enteral)

- Currently stocked at BWH (200 mg tablets)
- Dose: 400 mg BID x1 day, followed by 200 mg BID x4 days. May extend up to 10 days depending on clinical response
    - May use a maintenance dose of 200 mg TID in critically ill patients with hemodynamic instability or questionable drug absorption
    - Does not require renal adjustment for acute kidney injury, chronic kidney disease, or continuous renal replacement therapy
- Drug interaction checker
- Safety
    - Consider checking ECG prior to initiation given the risk of QT prolongation
    - Potential side effects: rash, blurry vision, headache, gastrointestinal symptoms
    - Potential serious toxicities: retinopathy, cardiomyopathy, myelosuppression, hemolytic anemia
- Literature: Yao 2020

Remdesivir (IV)

- Please discuss remdesivir trial enrollment with study team for key inclusion and exclusion criteria in the use for moderate or severe COVID-19 disease
- Compassionate use remdesivir cannot be utilized as BWH is an active trial site for NCT04292730 and NCT04292899
- Dose: 200 mg loading dose, followed by 100 mg daily
- Drug interaction checker
- Safety
    - Potential toxicities: elevated liver function tests
    - Co-formulated with sulfobutyl ether β-cyclodextrin (SBECD), so there is a theoretical risk of accumulation in renal failure promoting further renal injury, similar to intravenous voriconazole
- Literature: Wang 2020

Tocilizumab (IV)

- To be used only in patients with severe COVID-19 disease and suspicion of cytokine release syndrome in conjunction with infectious diseases consultation. Please order C-reactive protein (CRP), D-dimer, and interleukin-6 (IL-6) levels prior to treatment initiation as these may help guide treatment. Elevated IL-6 levels (>40 pg/mL) will take 3-4 days to result
- Limited supply at BWH
- Dose: typically 400 mg (4-8 mg/kg) x1, may repeat in 12 hours if needed for ongoing evidence of cytokine release syndrome
- Safety
    - Potential side effects: increased liver function tests, increased serum cholesterol, infusion-related reactions, neutropenia
    - Potential serious toxicities: theoretical risk of increased opportunistic infections (e.g. tuberculosis, invasive mycoses, herpes zoster, reactivation of latent HBV infections), gastrointestinal perforation, severe hepatotoxicity
- Literature: Xu 2020, Mehta 2020, information on status of potential clinical trials from Genentech

Medications that were considered for the management of COVID-19 at BWH, but are NOT currently recommended can be found on the next page

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Medications that were considered for the management of COVID-19 at BWH, but are NOT currently recommended

Angiotensin converting enzyme (ACE) Inhibitors or Angiotensin-receptor blockers (ARB)

- There are hypothetical arguments for and against use. We do not recommend initiating ACE-Is or ARBs in patients with COVID-19 at this time. However, we do not recommend stopping these agents in patients already on therapy either, per HFSA/ACC/AHA guidance

Baricitinib

- Not enough supporting evidence at this time
- Literature: Stebbing 2020, Richardson 2020

Chloroquine

- Long-term manufacturer backorder

Corticosteroids

- The CDC and WHO recommend against use of corticosteroids for COVID-19. Observational data for SARS and MERS suggest that there may be harm, despite potential benefit shown in one study. Corticosteroids should only be considered if indicated for other reasons (e.g. refractory septic shock). Consider discontinuation of inhaled steroids, unless patient is deemed at risk of exacerbation if the medication is discontinued

Darunavir/cobicistat or darunavir & ritonavir

- Ongoing trial in China (NCT04252274), but the manufacturer has come out and stated there is no data currently to support its use

HMG-CoA reductase inhibitors (statins)

- Not enough supporting evidence at this time to initiate therapy. However, patients already on therapy should continue their current regimen

Interferon Beta-1b

- While some *in vitro* studies and animal models suggest that interferon may have in vitro activity against other betacoronaviruses such as MERS-CoV, there are no data in humans showing efficacy of interferon treatment for SARS-CoV-2 or any other betacoronavirus infections

IVIG

- Prevalence of patients who have recovered from COVID-19 is likely very low in the blood donor population currently – pooled IVIG is unlikely to be useful for the management of patients with COVID-19

Lopinavir/ritonavir

- Long-term manufacturer backorder
- Literature: Cao 2020

Nitazoxanide

- Not enough supporting evidence at this time
- Literature: Wang 2020

Non-steroidal anti-inflammatory drugs (NSAIDs)

- Concern has been raised that NSAIDs may worsen COVID-19 disease. This has not been proven clinically to-date, so we cannot make a recommendation for or against their use at this time

Ribavirin

- Not enough supporting evidence at this time
- Literature: Arabi 2019, Chan 2013, Hart 2014, Falzarano 2013

Sarilumab

- Not currently available at BWH, but potential trial enrollment in a Phase 2/3 RCT in the future

Other therapies approved for other indications with **theoretical** effects vs. SARS-CoV-2 but **no preclinical or clinical data to support their use** in patients with COVID-19 include convalescent plasma, sofosbuvir/velpatasvir, nelfinavir, PARP inhibitors, siltuximab, sirolimus, paroxetine, melatonin, colchicine, and mercaptopurine.