| ZSFG Treatment Guidelines for Adults with confirmed COVID-19 | |
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| **Clinical scenario** | **Treatment recommended** |
| **ICU level care, with or without intubation** | • Consider available CLINCAL TRIALS:<br>- Mesenchymal stem cell (MSC) study if ARDS<br>Contact Critical Care team or Carolyn Hendrickson directly carolyn.hendrickson@ucsf.edu<br>- RDV via NIH study or other enrolling clinical trials (annie.luetkemeyer@ucsf.edu)<br>• IV remdesivir (RDV) x10 days (via emergency use authorization supply) if not feasible/appropriate to obtain through clinical trial.<br>• Consider convalescent plasma via expanded access program (EAP) if ARDS and critically ill, including need for prone positioning while mechanically ventilated<br>• Avoid steroids<br>• ARDS management per critical care team to include low tidal volume ventilation, fluid conservation, possible prone position. |
| **Hospitalized, non-ICU level care, moderate/severe disease[1]** | • IV remdesvir x 5 days (via emergency use authorization supply) if not feasible/appropriate to obtain through clinical trial<br>• Consider available clinical trials (annie.luetkemeyer@ucsf.edu)<br>• Consider convalescent plasma via EAP if severe immunocompromising condition |
| **Mild disease[1] (no hypoxia)** | • Consider available clinical trials<br>• Outpatient study referral line: English (415 942 2328) & Spanish (415 696 3392) |
| **Pregnant woman with severe disease[1]** | • Consider remdesivir via compassionate use<br>• Consider convalescent plasma via expanded access program |

[1]*Mild Disease: No radiographic abnormality, no hypoxia*
*Moderate disease:* Radiographic abnormality, O2 sat > 94% RA
*Severe Disease:* radiographic abnormality, O2 ≤ 94% on room or requiring supplemental oxygen/intubation or Pa02/Fi02 ≤ 300mmHg

**NOTE:** The COVID-19 ID treatment team does not recommend empiric hydroxychloroquine (with or without azithromycin) or antiretroviral therapies (e.g. lopinavir/ritonavir) outside of a clinical trial.

**Adjunctive therapies:**

- All hospitalized COVID-19 patients should be considered for VTE prophylaxis with LMWH, if no contraindication.
- There is no evidence to discontinue ACE inhibitors or ARBs that otherwise are indicated or to empirically start ACEI or ARBs in any stage of COVID-19 at this time.

## Overview

Remdesivir has shown efficacy in improving time to recovery and a trend towards mortality improvement and thus has become the current standard of care. The FDA has provided emergency use authorization (EUA) for remdesivir, thus available outside of clinical trials. However, given the current limited supply of RDV, enrollment into clinical trials is preferred when feasible and the RDV trials no longer have placebo arms. Given the availability of remdesivir as well as multiple clinical trials, off label therapies outside of clinical trials are not recommended for COVID treatment.

Please contact the ID/HIV team (pager 415 443 BUGS) for guidance regarding COVID-19 diagnosis and treatment and annie.luetkemeyer@ucsf.edu regarding available inpatient clinical trials. Outpatient study referral line: English (415 942 2328) & Spanish (415 696 3392)

## COVID-19 potential treatments

1. **Remdesivir:**
   A. Assess for inclusion in the NIH adaptive trial. Requires confirmed COVID-19 infection and at least one of the following (and may not be in other treatment trials for COVID-19):
      - Radiographic infiltrates by imaging (chest x-ray, CT scan, etc.), OR
      - Clinical assessment (evidence of rales/crackles on exam) AND SpO2 ≤ 94% on room air, OR
      - Requiring supplemental oxygen, OR requiring mechanical ventilation.

   B. Assess for exclusion
      - ALT/AST > 5 times the upper limit of normal
      - CrCl < 30 or ESRD on HD
      - Pregnancy or breastfeeding
      - Anticipated discharge within 72 hours
      - Currently enrolled in other COVID-19 treatment trials

   C. If remdesivir access through clinical trial is not an option, consider remdesivir though EUA or compassionate use. EUA RDV requires ID COVID team approval (Jain, Winston, Luetkemeyer). Compassionate use is currently only available for children < 18 and pregnant women with severe COVID-19. Contact annie.luetkemeyer@ucsf.edu (ZSFG) for compassionate use requests.

2. **Convalescent Plasma:**
   Convalescent plasma is available through an expanded access program for severe and critically ill patients. A single unit of ABO-compatible convalescent plasma is infused. At this time, given the lack of data for use in COVID-19 and limited availability of plasma from recovered patients, convalescent plasma should be reserved for those with ARDS who are critically ill, such as those with need for prone positioning during mechanical ventilation. Plasma also may be considered for hospitalized patients with COVID-19 with substantial immunocompromising conditions or medications, such as solid organ or stem cell transplant. When feasible, it is preferred to provide convalescent plasma through a clinical trial. Convalescent plasma is not an emergent intervention and should not be requested overnight- please discuss with the ID team during the day

3. **Anticoagulation**
   There are substantial data regarding hypercoagulable state associated with COVID infection, particularly in those receiving ICU level care. The American Society of Hematology recommends thromboprophylaxis with LWMH or fondaparinux (if history of heparin induced thromobocytopenia) for all hospitalized COVID patients, unless the risk of bleeding is judged to exceed the risk of thrombosis. Thomboprophylaxis with intermediate or therapeutic intensity anticoagulation is not recommended for hospitalized COVID patients *a priori* outside of clinical trials. Continuation of post discharge thromboprophylaxis for up to 40 days after discharge should be considered on a case by case basis, based on established risk factors for increased risk (age, D-Dimer > 2x ULN, comorbidities such as active cancer). For those who do not meet criteria for extended thromboprophylaxis, at minimum, aspirin use can be considered.
   *See ASH guidelines*: https://www.hematology.org/covid-19/covid-19-and-vte-anticoagulation

**NOTE: Hydroxychloroquine (HCQ)**

Hydroxychloroquine is FDA approved for other indications with limited in vitro data to suggest activity against COVID-19. At this point, there are no data to support clinical efficacy for COVID-19 treatment, although many clinical trials are underway. HCQ should only be used in the context of clinical trial.

**Medications/interventions to avoid**

- Steroids should be avoided unless otherwise indicated
- Avoid other pharmaceutical treatments (e.g. tocilizumab, ribavirin, interferon) specifically to treat COVID-19 unless part of a clinical trial
- ACEI/ARB inhibitors and NSAIDS should not be started or stopped on the basis of suspected/confirmed COVID-19 until further data available

**Considerations for COVID-19 treatments**

| **Convalescent Plasma** | |
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| Dosing | Single unit of ABO-compatible FFP from convalescent donor. |
| Important drug interactions | None |
| Pregnancy | Limited data for use of convalescent plasma in other diseases |
| Dose adjustment in renal dysfunction | No |
| Adverse effects | Potential for transfusion associated complications, including allergic reaction, transfusion association lung injury and (TRALI), transfusion associated circulatory overload (TACO), allergic reactions, and very rarely transmission of a blood borne pathogen |

| **Remdesivir** | |
|---|---|
| Dosing | 200mg IV x 1, then 100mg IV q24h for duration of hospitalization for up to 10 days |
| Dose adjustment in renal dysfunction | Not recommended if CrCl < 30 or dialysis – however, can be considered on case by case basis |
| Pregnancy/Lactation | Contraindication for clinical trial; available through compassionate use |
| Important drug interactions | Coadministration with strong CYP3A4 inhibitors is not recommended and coadministration with weak/moderate 3A4 inhibitors should be avoided if possible. |
| Adverse effects | Increased AST/ALT, reversible upon drug discontinuation. GI side effects, rash, renal failure due to cyclodextran excipient. |