Clinical Alignment Summary: COVID-19 Infectious Disease Treatment

The purpose of this summary is to display how clinical guidance from different organizations is aligned in this topic area.

### OVERVIEW
- There are no proven or approved treatments for COVID-19, all patients should receive standard supportive therapy.
- Risk stratify patients (Table 1).
- Patients with moderate to severe disease or at high risk for disease progression should be offered antiviral medications (Table 2).
- Avoid medications which have shown to be ineffective or harmful to patients with COVID-19 (Table 5).

#### TABLE 1. Risk factors for COVID-19 disease progression (3). The severity of COVID-19 is categorized into mild (symptoms but no dyspnea or abnormal imaging), moderate (lower respiratory disease w/ SpO2 >94% on room air), severe* (SpO2 ≤ 94% on room air, requiring supplemental oxygen, mechanical ventilation, or extracorporeal membrane oxygenation). These definitions vary in the literature (3)

<table>
<thead>
<tr>
<th>Epidemiological – Category 1</th>
<th>Vital Signs – Category 2</th>
<th>Labs – Category 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 55</td>
<td>Respiratory rate &gt; 24 breaths/min</td>
<td>D-dimer &gt; 1000 ng/mL</td>
</tr>
<tr>
<td>Pre-existing pulmonary disease</td>
<td>Heart rate &gt; 125 beats/min</td>
<td>CPK &gt; twice upper limit of normal</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>SpO2 ≤94% on ambient air</td>
<td>CRP &gt; 100 mg/L</td>
</tr>
<tr>
<td>Diabetes with A1c &gt; 7.6%</td>
<td>PaO2/FiO2 &lt; 300 mmHg</td>
<td>LDH &gt; 245 U/L</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>Admission absolute lymphocyte count &lt; 0.8 K/ul</td>
<td>Elevated troponin</td>
</tr>
<tr>
<td>History of cardiovascular disease</td>
<td></td>
<td>Ferritin &gt; 500 ug/L</td>
</tr>
<tr>
<td>Use of biologics**</td>
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<tr>
<td>History of transplant or other immunosuppression** including chronic corticosteroid &gt;20 mg/d of prednisone</td>
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<tr>
<td>HIV with CD4 cell count &lt;200 or unknown**</td>
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</tbody>
</table>

**Not yet proven as risk factors for progression, inferred from other infections. Other factors include poverty, racism, recent cancer chemotherapy, recent surgery (3)

#### TABLE 2. Recommended antiviral therapy

**Remdesivir**
- Appears to demonstrate the most benefit in those with severe COVID-19 on supplemental oxygen rather than in patients on mechanical ventilation or extracorporeal mechanical oxygenation (4)
- In situations where supplies are limited, recommends prioritized for use in hospitalized patients with COVID-19 who require supplemental oxygen but who are not mechanically ventilated or on ECMO (5)
- Recommended for treatment of COVID-19 in hospitalized patients including pregnant patients with severe* disease (1,2,3)
- Insufficient data to recommend for or against for the treatment of patients with mild or moderate COVID-19 (3,5)

<table>
<thead>
<tr>
<th>Emergency Use Authorization (EUA)</th>
<th>FDA authorized emergency use on May 1, 2020.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergency Use Criteria</td>
<td>SpO2 ≤94% on ambient air (at sea level), requiring supplemental oxygen, mechanical ventilation, or extracorporeal membrane oxygenation</td>
</tr>
<tr>
<td>Compassionate Use</td>
<td>Consider for hospitalized children &lt;18 yo with confirmed CoVID-19 and severe manifestation of disease (1,3). Pregnant patients who do not meet EUA criteria (3)</td>
</tr>
<tr>
<td>Clinical trial exclusion criteria</td>
<td>AST/ALT &gt; 5x upper limit of normal, CrCl &lt; 50 mL/min, eGFR &lt; 30 or requiring dialysis, continuous veno-venous hemofiltration, or previous hypersensitivity</td>
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<tr>
<td>Mechanism/target</td>
<td>RNA dependent RNA polymerase inhibitor</td>
</tr>
<tr>
<td>Toxicity</td>
<td>Nausea, vomiting, increased AST/ALT, reversible kidney injury, hypotension during infusion</td>
</tr>
</tbody>
</table>

**TABLE 3. Other recommended medications**

**Dexamethasone**
- Recommended for patients who are mechanically ventilated and those on supplemental O₂ (3,4,7)
- There is no data to support the use of dexamethasone and remdesivir in combination, but co-administration is allowable (3)

**TABLE 4. Other therapies**

**Hydroxychloroquine/ chloroquine**
- Recommended only in the context of a clinical trial (3,4,5)
- Chloroquine has activity, but due to safety concerns should not be used (3)
- Chloroquine antagonizes remdesivir in vitro against RSV. Chloroquine and HCQ should not be co-administered with remdesivir (3)
- The use of hydroxychloroquine plus azithromycin for the treatment of COVID-19 is not recommended, except in the context of a clinical trial (4,5)

**IL-6 inhibitors:**
- **Tocilizumab**
  - Recommended against routine use (1), only in context of a clinical trial (1,2,4)
  - Insufficient clinical data to recommend either for or against (6)

**IL-1 inhibitors:**
- **Anakinra**
  - Insufficient clinical data to recommend either for or against (6)

**Intravenous Immune Globulin (IVIG)**
- Insufficient data for the COVID-19 Treatment Guidelines Panel (the Panel) to recommend either for or against the use of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) immunoglobulins (6)
- Non-SARS-CoV-2-specific intravenous immune globulin (IVIG) not recommended, except in the context of a clinical trial (1,6).
- This should not preclude the use of IVIG when it is otherwise indicated for the treatment of complications that arise during the course of COVID-19 (6), including multisystem inflammatory syndrome (3)

**Convalescent Plasma**
- Recommended only in context of a clinical trial (2,4)
- Consider expanded access program for severe respiratory failure or severe immunocompromise. Optimal patient selection, timing of administration in course of illness and clinical benefits are under investigation (1,2)
- Insufficient clinical data to recommend either for or against (6)

**Statins**
- Continue statins if already prescribed (3,7)
- For those who have a guideline indication, and if no contraindication (e.g. pregnancy), consider starting atorvastatin 40 mg daily (3)
- NIH does not recommend statin therapy as treatment for COVID-19 outside a clinical trial (7)
Lopinavir/Ritonavir

- Not recommended (1,3) or considered only in context of clinical trial (2,4,5)

Ribavirin

- Not recommended (3) or considered only in context of clinical trial (2)

Interferons

- Recommended only in the context of a clinical trial (2,6)

**TABLE 5. Medications not currently recommended**

**Antibiotics**

- Avoid routine empiric antibiotics (1,3)
- For patients for whom antibiotics are indicated for presumptive secondary bacterial pneumonia, ceftriaxone and doxycycline is preferred over azithromycin in non-pregnant patients (3)

**Other medications**

- Dexamethasone is not recommended for patients who do not require O₂ support unless there is another indication for corticosteroids (3,4,7)
- Ivermectin (should be reserved for other FDA approved indications) (1,3)
- ACE inhibitors and ARB's are not recommended outside standard indications (3) or outside a clinical trial (7).
- American Heart Association, Heart Failure Society of America, and American College of Cardiology all recommend that ACE inhibitors or ARBs be continued in people who have an indication for these medications

**Recommendations are aligned across institutions/organizations with the exceptions as marked:**

**SOURCES**

2. University of California at San Francisco Inpatient Adult COVID-19 Management Guidelines, Updated 7/1/20
3. Massachusetts General Hospital COVID-19 Treatment Guidance, Updated 7/1/20
4. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19, Updated 6/22/20
7. NIH COVID-19 Treatment Guidelines: Considerations for Certain Concomitant Medications in Patients with COVID-19, Updated 7/17/20

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