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 experimental antiviral medications (Table 2).
- Avoid medications which have shown to be ineffective or harmful to patients with COVID-19 (Table 3).

TABLE 1. Risk factors for COVID-19 disease progression (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>
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<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>
<td></td>
<td></td>
</tr>
<tr>
<td>History of transplant or other immunosuppression**</td>
<td>including chronic corticosteroid &gt;20 mg/d of prednisone</td>
<td></td>
</tr>
<tr>
<td>HIV with CD4 cell count &lt;200 or unknown**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>**Not yet proven as risk factors for progression, inferred from other infections.</td>
<td></td>
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</tbody>
</table>

TABLE 2. Experimental Antiviral Therapy:

Consider the following antiviral therapies for patients with moderate to severe disease, or high risk for disease progression (any category 2 or 3 feature, Table 1), or requiring supplemental oxygen or mechanical ventilation (1,2,3).

Remdesivir
- Recommended for treatment of COVID-19 in hospitalized patients with severe disease; for moderate disease, not recommended outside of clinical trial (1,3,5)

Emergency Use Authorization (EUA) | FDA authorized emergency use on May 1, 2020.
Emergency Use Criteria | SpO2 ≤94% on ambient air (at sea level), requiring supplemental oxygen, mechanical ventilation, or extracorporeal membrane oxygenation
Clinical trial exclusion criteria | AST/ALT>5x upper limit of normal, CrCl<50mL/min, eGFR<30 or requiring dialysis, or continuous veno-venous hemofiltration
Mechanism/target | RNA dependent RNA polymerase inhibitor
Toxicity | Nausea, vomiting, Increased AST/ALT, reversible kidney injury, hypotension during infusion

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TABLE 3. Medications not currently recommended

**Hydroxychloroquine/Chloroquine**
- Routine use is no longer recommended outside of a randomized clinical trial (1)
- Recommended only in context of a clinical trial (4)
- Insufficient clinical data to recommend either for or against; recommend against using high-dose chloroquine for the treatment of COVID-19 (5)

<table>
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<tr>
<th>Mechanism/target</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple actions; prevents binding to ACE2, prevents transport in endosome, possibly others</td>
<td>QTc-prolonging drug. Given the growing evidence of myocarditis and arrhythmias with COVID, HCQ should be used with caution in this group of patients. Check ECG prior to initiation. Co-administration with azithromycin not recommended (1,5) or only in context of clinical trial (4). Avoid use in patients with G6PD deficiency due to risk of hemolytic anemia (2).</td>
</tr>
</tbody>
</table>

**Antivirals**
- Lopinavir/Ritonavir (1) OR consider only in context of clinical trial (1, 2, 4, 5)
- Ribavirin±Interferon (1, 2)
- Interferon (1, or outside a clinical trial 5)

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

**Other medications**
- Routine use of corticosteroids (1, 2, 3, 4, 7) (only consider in context of clinical trial for patients with ARDS 4, or low dose in refractory shock 7)
- Ivermectin (It should be reserved for other FDA approved indications) (1,3)
- ACE inhibitors and ARB’s are not recommended outside standard indications (1, 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

**Tocilizumab**
- Until more data are available, use of tocilizumab in patients with severe or life-threatening COVID-19 is NOT recommended except in a shared decision-making context with ID and Pulmonary/Critical Care in patients with severe disease exhibiting clinical deterioration despite use of empiric antiviral treatment and supportive care (1)
- Consider with ID input for patients with evidence of cytokine release syndrome (3)
- Recommended only in context of a clinical trial (4)
- Insufficient clinical data to recommend either for or against (6)

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<td>Monoclonal antibody to IL-6 receptor</td>
<td>ALT elevations, decline in neutrophils, bowel perforation if history of diverticulitis</td>
</tr>
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</table>

**Note:**
- **Convalescent Plasma:** Recommended only in context of a clinical trial (1,4). Insufficient clinical data to recommend either for or against (6).
- **Statins:** Continue statins if already prescribed. For those who have a guideline indication for a statin and if no contraindication (e.g. pregnancy), consider starting atorvastatin 40 mg daily (3).
- NIH does not recommend statin therapy as treatment outside a clinical trial (7).
Recommendations are aligned across institutions/organizations with the exceptions as marked:

**SOURCES**

1. University of Washington Medicine COVID-19 Treatment Guidelines, Updated 5/19/20
2. University of California at San Francisco Inpatient Adult COVID-19 Management Guidelines, Updated 4/6/20
3. Massachusetts General Hospital COVID-19 Treatment Guidance, Updated 5/19/20
4. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19, Updated 4/21/20
7. NIH COVID-19 Treatment Guidelines: Considerations for Certain Concomitant Medications in Patients with COVID-19, Updated 4/21/2020

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