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Frequently Asked Questions for COVID Management Support Document

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1) Which patients should I start on hydroxychloroquine (HCQ)?
   In general, we recommend starting hydroxychloroquine only for hospitalized patients with Category 2 or 3 risk factors for severe COVID disease (see table 2 in appendix or in guidance document). This includes individuals with vital sign or significant laboratory abnormalities.
   Please note that HCQ is an unproven therapy for COVID-19.

2) Should hydroxychloroquine be given for longer than 5-days?
   We recommend against giving hydroxychloroquine for longer than 5 days or at a higher dose than the standard dose of 400 mg q12hours x2 doses, then 400mg daily for 4 additional days (5-days total, unless discharged from hospital). The half-life of hydroxychloroquine is > 3 weeks.
Longer durations may place patients at risk for toxicity without known added benefit for treatment of COVID-19.

3) What is the QTc?

The QTc is an interval on an electrocardiogram (ECG) measured in milliseconds. A normal QTc is ≤ 470 ms for males and ≤ 480 ms for females. A prolonged QTc may place a patient at a higher risk for an abnormal cardiac rhythm. Certain drugs prolong QTc, and therefore QTc needs to be monitored closely.

All COVID-19 patients starting on hydroxychloroquine should have a baseline ECG. If they have a prolonged QTc at baseline (particularly if QTc > 500 ms), then hydroxychloroquine should not be started without talking with a cardiologist.

4) How to monitor QTc?

Please refer to guidance document on QTc monitoring.

5) Should ceftriaxone and azithromycin be started on my patient?

In general, we do not recommend empiric addition of azithromycin to HCQ for all patients with COVID-19. There are no good data supporting the role of azithromycin for COVID-19 at this time and both agents prolong QTc and put patients at risk for cardiac arrhythmias.

Ceftriaxone (IV 1 g daily) with azithromycin (500 mg x1, then 250 mg daily x4 days) is the standard empiric treatment for bacterial community acquired pneumonia. We do not recommend starting this on all patients with confirmed COVID-19. It can be considered on a case by case basis if the primary care team is worried about bacterial superinfection or if the diagnosis of COVID-19 is not clear. Whether antibacterial agents should be continued may be reassessed on a daily basis.

A procalcitonin < 0.25 ng/mL is most consistent with a viral pneumonia. In COVID-19 a higher pro-calcitonin does not necessarily indicate a bacterial pneumonia, although it is reasonable to try to obtain a sputum culture for these patients and some may warrant antibiotics.

6) Can I give steroids to my patient with asthma or COPD?

We currently do not recommend routine steroid administration for COVID patients. However, those with other indications for steroids (including COPD and asthma exacerbations) can receive the usual steroid regimen for these issues. In general wheezing seems to be unusual for COVID alone and should raise suspicion for a concomitant condition such as asthma or COPD (which might require steroids).
7) For which patients should I order a procalcitonin?

Procalcitonin does not have to be ordered routinely on all patients with COVID-19. Procalcitonin is a serum biomarker that has some utility in distinguishing viral from bacterial infections, particularly of the lower respiratory tract. From COVID studies to date, procalcitonin seems to remain low in the first 7-10 days of symptoms and can rise later on, even without bacterial superinfection.

It may be helpful in at least 2 situations: first, if a patient with COVID-19 is presenting with a short duration of symptoms and there is concern for possible bacterial pneumonia, a low value would be reassuring at that point in terms of not requiring systemic antibiotics. Additionally, if a patient has clinical progression or worsening a low value (< 0.25) in the setting of clinical deterioration would make bacterial superinfection less likely. However, a higher value has less specificity later in the disease course as they could be consistent with either progressive COVID or bacterial superinfection.

8) What are the guidelines indications for stating a statin?

Patients with guidelines indications for statins include those with known coronary artery disease, those with hyperlipidemia with an ACC/AHA 10-year risk score > 10% (see online calculator for: Cardiovascular risk assessment in adults 10-year, ACC/AHA 2013) and those with diabetes. Additional risk factors for cardiovascular disease where statins may be considered include hypertension, cigarette smoking, premature family history of CVD, chronic kidney disease, obesity, and people living with HIV or other chronic infections.

9) How to find an active COVID-19 treatment clinical trial at MGH?

COVID-19 treatment trials are being updated on a daily basis. Study teams are constantly searching the list of active COVID-19 patients for patients to enroll and will approach the primary clinical team if they think your patient is a good candidate. If you think your patient is a candidate for a specific trial and have not heard from the study team, please reach out to the study coordinator of each trial. The updated list with active trials, including eligibility criteria, is below in the appendix under Table 3.

10) How do I know if my patient with COVID is ready for discharge?

There are no universal discharge criteria for patients with COVID. We recommend cases be considered on an individual basis by primary care teams.

We recommend looking at:
- MGH COVID Floor Operations
• In general, we recommend that patients have a general trend of clinical improvement and be off supplemental oxygen (or on their baseline amount of O2), with improving laboratory studies.

11) What do I do with hydroxychloroquine or other medications started for COVID for patients discharged before they complete their course?

Hydroxychloroquine should be discontinued at the time of discharge, because the patient is improving, HCQ has a long half-life, and there is no established duration. If the suspicion for bacterial superinfection is low, antibiotics such as ceftriaxone and/or azithromycin may also be discontinued.

12) What should I do about statins that were started in the hospital for patients with COVID?

If a patient has a primary care provider and a good follow up plan, statins can be continued after discharge, if the primary care team communicates the plan with the patient’s primary care provider.
## Appendix

Table 2: Risk Factors for Severe Disease

<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 ≤ 93% on ambient air</td>
<td>CRP &gt; 100</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></td>
<td>Elevated troponin</td>
</tr>
<tr>
<td>History of cardiovascular disease</td>
<td></td>
<td>Admission absolute lymphocyte count &lt; 0.8</td>
</tr>
<tr>
<td>Use of biologics*</td>
<td></td>
<td>Ferritin &gt; 500 ug/L</td>
</tr>
<tr>
<td>History of transplant or other immunosuppression*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV, CD4 cell count &lt;200 or unknown CD4 count*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Table 3: COVID-19 Treatment Trials for Inpatients at the Massachusetts General Hospital**

<table>
<thead>
<tr>
<th>Investigational Agent</th>
<th>Protocol</th>
<th>Site PI</th>
<th>Study Coordinator</th>
<th>Status</th>
<th>Contact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remdesivir&lt;sup&gt;i&lt;/sup&gt;</td>
<td>ACTT</td>
<td>Dr. Libby Hohmann</td>
<td>Mariam Torres</td>
<td>Open</td>
<td><a href="mailto:MTORRESSOTO@mgh.harvard.edu">MTORRESSOTO@mgh.harvard.edu</a></td>
</tr>
<tr>
<td>Sarilumab&lt;sup&gt;ii&lt;/sup&gt;</td>
<td>6R88-COV-2040</td>
<td>Dr. Michael Mansour</td>
<td>Natalie Atallah</td>
<td>Open</td>
<td><a href="mailto:NATALLAH@mgh.harvard.edu">NATALLAH@mgh.harvard.edu</a></td>
</tr>
<tr>
<td>Nitrous Oxide&lt;sup&gt;iii&lt;/sup&gt;</td>
<td>NOSARSCOVID</td>
<td>Dr. Lorenzo Berra</td>
<td>Raffaele Di Fenza</td>
<td>Open</td>
<td><a href="mailto:RDIFENZA@mgh.harvard.edu">RDIFENZA@mgh.harvard.edu</a></td>
</tr>
</tbody>
</table>

<sup>i</sup>Eligibility Criteria for Remdesivir:

**Inclusion Criteria:**
- ≥ 18 years old in hospital with symptoms suggestive of COVID-19 infection.
- Has laboratory-confirmed SARS-CoV-2 < 72 hours prior to randomization.
- Illness of any duration, and at least one of the following: radiographic infiltrates by imaging (chest x-ray, CT scan, etc.), clinical assessment (evidence of rales/crackles on exam) AND SpO2 ≤ 94% on room air, requiring supplemental oxygen, requiring mechanical ventilation

**Exclusion Criteria:**
- ALT/AST > 5 times the upper limit of normal.
- Estimated glomerular filtration rate (eGFR) < 50 or requiring dialysis.
- Pregnancy or breast feeding.
- Anticipated transfer to another hospital which is not a study site within 72 hours.

<sup>ii</sup>Eligibility Criteria for Sarilumab:

**Inclusion Criteria:**
- ≥ 18 years old in hospital
- Illness of any duration with evidence of pneumonia and severe disease, critical disease, or multi-system organ dysfunction at baseline
- Ability to provide informed consent by study patient or legally acceptable representative

**Exclusion Criteria:**
- In opinion of investigator, unlikely to survive > 48 hours from screening
- ANC < 2000/mm3, AST/ALT > 5x ULN, PLT < 50,000/mm3
- Treatment with anti-IL 6, anti-IL-6R antagonists or with JAK inhibitors in the past 30 days or plans to receive during the study period
- Current treatment with simultaneous combination of leflunomide and methotrexate
- Known or suspected active tuberculosis
- Suspected or known systemic bacterial or fungal infections
- Receipt of immunosuppressive antibody therapy within the last 5 months, including IVIG
- Participation in a clinical research study in the past 3 months (COVID-19 treatments in context of open-label or compassionate use study are permitted)
- Any findings that, in the opinion of the investigator, might confound results or pose additional risk to the patient
- Known systemic hypersensitivity to sarilumab

Eligibility Criteria for Nitrous Oxide:

Inclusion Criteria:
- ≥ 18 years old in hospital with symptoms suggestive of COVID-19 infection.
- Intubation and mechanical ventilation
- Documented positive SARS-CoV-2 by RT-PCR

Exclusion Criteria:
- Intubated for > 72 hours at time of initiation of NO treatment
- Pregnancy