Infectious Disease Division Guidance for COVID-19 Patients

Last updated 3/30/20

INTRODUCTION

The mainstay of treatment for COVID-19 is supportive therapy. There are no FDA approved or known effective therapies for COVID-19. CDC\(^1\) and WHO\(^2\) guidelines recommend supportive care as the standard of care.

Our recommendation, in line with that of the WHO is that investigational anti-COVID-19 therapeutics should be used only in ongoing randomized, controlled trials\(^2,3\). Currently at Stanford we are enrolling patients in clinical trials of remdesivir\(^4,5\), a novel anti-viral agent.

This guidance will be updated frequently as new clinical trials start at Stanford and as clinical trial data become available from other centers.

Remdesivir Randomized Controlled Trials at SHC

Each COVID-19 patient will be assessed for eligibility for a randomized controlled trial of remdesivir, a RNA polymerase inhibitor as soon as their COVID-19 test results positive. The triage process (see COVID treatment algorithm) for eligibility is currently done by the ID team.

Exclusion criteria (subject to change): Pregnancy, AST/ALT ≥ 5x ULN, CrCl <50 mg/ml and multi-system organ failure.

To access remdesivir, call the Infectious Disease consult services at:

General ID 24308 | ICU ID 27190 | BMT ID 17000 | SOT ID 17008

Please note that starting patients on hydroxychloroquine or other investigational agents targeting COVID-19 (other than standard supportive care) will delay their entry into the remdesivir clinical trial by 24h.

If the patient is on a clinical trial, orders for the study drug will be placed by the investigational pharmacy (650-736-1990). Except in an emergency, please do not stop the study drug without first discussing with the study team (page COVID19 or 15013)
Remdesivir

<table>
<thead>
<tr>
<th>Dosing</th>
<th>200 mg IV x1 then 100 mg IV daily x 4-9 days</th>
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</thead>
<tbody>
<tr>
<td>Dose adjustment in renal dysfunction</td>
<td>Hold if CrCl decreases by $\geq 50%$ from baseline</td>
</tr>
<tr>
<td>Known side effects</td>
<td>Transient elevation of AST/ALT, and Cr. Nausea</td>
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For patients ineligible for remdesivir or other drugs as part of a clinical trial, we do not recommend unproven experimental therapies, though they may be considered on a case by case basis.

**Non-evidenced based potential therapies for COVID-19**

A helpful review of early and emerging potential therapies for COVID-19\(^7\) is available [here](#).


i. *Hydroxychloroquine* – this antimalarial and anti-inflammatory drug has activity *in vitro* against SARS-CoV-2\(^7\).

Anecdotal data show possible benefit, but it was not effective for COVID19 in one small (n=30), poor quality, clinical trial\(^8\). A recent emergency use authorization (EUA) issued on 3/28/20 allows healthcare facilities to access this medicine from the national stock pile. It does not imply that this medicine is FDA approved for treating COVID-19 and in fact the EUA specifies that it is not. G6PD deficiency testing is NOT needed before starting this agent. Poryphyria and QTc > 500 ms are contraindications. Using hydroxychloroquine will cause a delay of 24h of entry into the remdesivir clinical trial. Use of hydroxychloroquine should occur after consultation with ID colleagues. If implemented, suggested dosing is a loading dose of 400 mg PO q 12hrs x 2 doses followed by 400 mg per day (given daily or as 200 mg BID). Daily dosing preferred for reduced nursing interactions with patient but twice daily dosing can be used if patient experiences GI intolerance.”

ii. *Nitazoxanide* – this anti-parasitic agent has *in vitro* activity against SARS CoV-2\(^9\). It is being investigated for the management of influenza and other acute respiratory infections at a dose of 600 mg PO BID\(^6\) as well as for enteric viruses (e.g. norovirus and sapovirus) at 500 mg PO BID. FDA approved dosing for diarrhea caused by Cryptosporidium is 500 mg PO BID x 3 days.
iii. **Chloroquine** – this antimalarial agent has activity *in vitro* against SARS-CoV-2 but significantly more side effects than hydroxychloroquine including QTc prolongation, arrhythmias, nausea and tinnitus. There are no good quality RCT data showing efficacy, but multiple clinical trials are ongoing in China. Given the lack of evidence and side-effects, the ID division recommends against this at this time.

iv. **Tocilizumab** – this IL-6 antagonist is currently undergoing clinical trials in Europe, Asia and the US. Anecdotal evidence suggests a possible benefit in patients with very high IL-6 levels. Given the lack of evidence and side-effects, the ID division recommends against this at this time.

v. **Azithromycin** – In a small (n=36), poorly designed (non-randomized, with controls n=16) including patients who declined to participate and patients at a non-participating hospital) single arm study looking at the effects of HCQ 200 mg TID (n=20) on viral eradication for COVID-19 in outpatients, 6 patients who received HCQ were also prescribed azithromycin. The investigators found viral eradication was numerically superior in this subgroup (6/6, 100%) compared to those who received hydroxychloroquine alone (8/14, 57%). However, there are numerous flaws in this study which may invalidate these findings. Given the lack of evidence and risk of side effects (including QT prolongation and diarrhea), the ID division recommends against this at this time.

vi. **Lopinavir/ritonavir** – this HIV protease inhibitor was studied two small randomized clinical trials (n=30 and n=44) and showed no benefit. Given the lack of evidence and side-effects (diarrhea and drug-drug interactions), the ID division recommends against this at this time.

vii. Investigations of many other agents are ongoing and this guidance will be updated frequently. A list of ongoing clinical trials worldwide is available here [http://med.stanford.edu/id/covid19.html](http://med.stanford.edu/id/covid19.html).
References:


