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COVID-19 treatment: a primer

MGH-ID-CHANT Team
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Purpose

• This document was developed by ID for frontline clinicians and staff at MGH and pertains to hospitalized patients
• It aims to provide:
  • Quick basics about medication management and common treatment options
  • Talking points for patients and family
• It does not cover issues related to infection control, PPE, supportive care, and ICU management
• Please refer to the central MGH-ID-CHANT document on the Apollo DOM website for more details
• This will be a living presentation that will be updated as more treatments become available
COVID-19 Disease Course

SARS-CoV-2 Respiratory Viral RNA Load

Antibodies turn positive 6-12 days after symptom onset

<table>
<thead>
<tr>
<th>Incubation Period</th>
<th>Acute Mild Phase *</th>
<th>ARDS/Pro-inflammatory Phase</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.1 days (median)</td>
<td>5-10 days</td>
<td>Days - weeks</td>
<td></td>
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</tbody>
</table>

Symptom onset

Hallmarks: dyspnea, tachypnea, hypoxemia

* Acute Mild Phase: nonspecific symptoms. Most commonly fevers, cough, myalgias, fatigue. Nausea, diarrhea reported <50% of the time

Pan Lancet ID 2020 https://doi.org/10.1016/S1473-3099(20)30113-4
Zou NEJM 2020 DOI: 10.1056/NEJMct2001737
Zhou Lancet 2020 https://doi.org/10.1016/S0140-6736(20)30566-3
Li NEJM 2020 DOI: 10.1056/NEJMoa2001316

Siddiqi JHLT 2020 doi:10.1016/j.healun.2020.03.012
Wolfel Nature doi:10.1038/s41586-020-2196-x
General treatment talking points for patients

• MGH is using best practices for “supportive care” such as oxygen, lab monitoring and nursing care
• We closely look at your prior medications and maintain ones that we feel are important for your health
• There are no proven treatments for COVID-19
• We may add treatment that may someday be proven to:
  • Help with the complications of COVID-19
  • Slow down the virus that causes COVID-19
  • Dampen the overreaction of your immune system during COVID-19
Hydroxychloroquine

- Hydroxychloroquine (HCQ) is a medication that has been used for a long time in diseases such as rheumatoid arthritis, lupus, and malaria
- Scientists in the laboratory showed that HCQ inhibits SARS-CoV-2 (the virus that causes COVID)
- It is not yet proven to be effective with high standard medical evidence
- HCQ is relatively safe when used for short term, major concern may be QT prolongation, especially in combination with other agents
- It is being used and studied for certain people with severe or progressive COVID around the world
- It is related to chloroquine but may be safer
- HCQ has a long half-life; it should not be extended beyond 5 days, and it may be discontinued at the time of discharge even if the patients has received fewer than 5 days

Wang et al. Cell Research 2020
Hydroxychloroquine talking points for patients

• Hydroxychloroquine has been used by many people all over the world for diseases like lupus and malaria
• Hydroxychloroquine may slow the virus in your body’s cells and decrease excessive inflammation which may also be helpful
• Hydroxychloroquine is not yet proven to be helpful for COVID-19 but is being used in many people around the world
• We will monitor your labs and do electrocardiograms to be sure this medication can be given safely
Remdesivir

- Remdesivir is an investigational drug that is available at MGH via a study
  - It is also available for children and pregnant women via compassionate use (apply https://rdvcu.gilead.com/)
- Remdesivir is a nucleotide prodrug that inhibits RNA-dependent RNA polymerase, the enzyme that is necessary to copy the genetic information of SARS-CoV-2, the virus that causes COVID-19
- Inhibitors of viral polymerases are used against other viruses such as HIV, HCV, and herpesviruses. Remdesivir has activity against Ebola and other coronaviruses
- Some patients can develop elevated LFTs on this medication
- Acetaminophen is not to be used if on the study; ibuprofen may be considered for fever reduction

Remdesivir works like many antivirals that target the viral polymerase enzyme
Remdesivir talking points for patients

• You may be receiving remdesivir, a drug not approved by the FDA, but is being studied for COVID-19
• Remdesivir directly slows down the part of the virus that makes new copies of itself
• It is not yet proven to be helpful, but shows promise based on studies in the laboratory and it has been used for treating other viruses
• You are being monitored closely for side effects
Favipiravir

- Favipiravir is an investigational drug that is available at MGH via a study
- Favipiravir is a prodrug that after metabolism inhibits RNA-dependent RNA polymerase, the enzyme that is necessary to copy the genetic information of SARS-CoV-2, the virus that causes COVID-19
- Inhibitors of viral polymerases are used against other viruses such as HIV, HCV, and herpesviruses. Favipiravir has activity against influenza and coronaviruses
- It is approved in Japan since 2014 and China since 2020 for influenza, but not by the FDA
- There are concerns about teratogenic effects in animal studies, so pregnant women are excluded
- It is generally well tolerated; GI side effects such as diarrhea may occur.
- Favipiravir is associated with elevated uric acid levels
Favipiravir talking points for patients

• You may be receiving favipiravir, a drug not approved by the FDA, but is being studied for COVID-19
• Favipiravir directly slows down the part of the virus that makes new copies of itself
• It is not yet proven to be helpful, but shows promise based on studies in the laboratory and it has been used for treating other viruses
• You are being monitored closely for side effects
Statins

• Statins are very common medications that help control lipids and also have anti-inflammatory properties
• Many of the risk factors for severe COVID are indications for statins (heart disease, diabetes, etc.)
• COVID can also be associated with vascular and cardiac inflammation
• Statins have been studied and are safe in the setting of infection and inflammation
• Statins are associated with less severe viral pneumonia from influenza

Yuan 2015 DOI: 10.1128/mBio.01120-15

A proposed anti-inflammatory mechanism in the setting of MERS, a viral infection similar to COVID
Statin recommendations

• Don’t stop statins if patients are already on them
• Consider starting for some patients that have cardiac risk factors
• Don’t start statins just for COVID-19
• At discharge, continue the statin if it was a preexisting medication, or if started in the hospital for cardiac risk if there is an adequate follow-up plan
Statin talking points for patients

• Statins are common medications used to protect the heart (from heart attacks) and brain (from strokes)
• Statins are not a treatment for the virus, but they may protect you from heart complications
• Statins are safe, we will monitor you closely for any effects
Sarilumab and tocilizumab

- Sarilumab and tocilizumab are both antibodies to the receptor for interleukin 6 (IL-6)
- IL-6 is a protein that the body makes when it is inflamed
- Sarilumab and tocilizumab do not block the virus directly
- Sarilumab and tocilizumab are likely safe, especially with short-term use
- In China, a group of 21 patients who received a drug called tocilizumab (similar to sarilumab) had improvement in their fevers, markers of inflammation and needed less extra oxygen. In the group who received that drug, there were no serious side effects seen
- It is being studied to see if these drugs help people feel better faster, but their efficacy is unknown
Sarilumab / tocilizumab talking points for patients

- You may be receiving sarilumab or tocilizumab which are drugs used for other reasons and approved by the FDA but are being studied for COVID-19.
- The immune system may react strongly to the virus that causes COVID-19.
- Part of that reaction includes a lot of a “cytokine” that is made by immune cells. Some think high amounts of this cytokine cause problems.
- Sarilumab and tocilizumab both directly block the effects of this cytokine.
- You are being monitored closely for side effects.
Nitric Oxide for Mild Disease (non-ICU)

- Nitric oxide (NO) is a gas that when inhaled relaxes the smooth muscle of the pulmonary vasculature and is used to improve oxygenation.
- NO was used during the first SARS epidemic.
- In vitro, NO-donor molecules exert direct antiviral effects against SARS-CoV.
- For this trial, it is delivered via a modified non-rebreathing mask using a tight facemask. All breaths will be captured and cleared by an antiviral HEPA filter.
- The treatment lasts for 30 minutes BID for 14 days or until discharge, intubation or absence of symptoms for 3 days.
Nitric oxide talking points for patients

• The air you breathe is mostly made up of nitrogen and oxygen
• Nitric oxide is a special combination of nitrogen and oxygen. After you inhale this combination, it may improve the blood flow through your lungs
• In the laboratory, nitric oxide slows down the virus that caused the first SARS epidemic, which is closely related to the virus that causes COVID-19
• Nitric oxide is generally safe, and we will monitor you during and after the inhalation
• You will receive this inhalation twice a day
Other medications

- We generally recommend **avoiding** initiation of systemic steroids\(^1\) and not starting inhaled steroids in those without lung disease
  - Patients with COVID-19 who also have chronic lung disease should be discussed with a lung specialist
- There are **no data** regarding the safety or harm of NSAIDs, despite anecdotal some reports
  - Continue those on chronic NSAIDs, guided by indication and status
  - Generally acetaminophen is preferred in hospitals for fever reduction, if NSAIDs are used, please administer the lowest effective dose
- Currently there are **no convincing data** to support either starting or stopping ACEi/ARBs on any patients with COVID-19. We do not currently routinely recommend stopping these agents for patients with COVID-19. We also do not recommend starting them at this time.
- There are no convincing data for adding **azithromycin** to HCQ for COVID-19. Azithromycin may be used if there is another indication for its use.