This document was prepared (in March-November, 2020) by and for MGH medical professionals (a.k.a. clinicians, care givers) and is being made available publicly for informational purposes only, in the context of a public health emergency related to COVID-19 (a.k.a. the coronavirus) and in connection with the state of emergency declared by the Governor of the Commonwealth of Massachusetts and the President of the United States. It is neither an attempt to substitute for the practice of medicine nor as a substitute for the provision of any medical professional services. Furthermore, the content is not meant to be complete, exhaustive, or a substitute for medical professional advice, diagnosis, or treatment. The information herein should be adapted to each specific patient based on the treating medical professional’s independent professional judgment and consideration of the patient’s needs, the resources available at the location from where the medical professional services are being provided (e.g., healthcare institution, ambulatory clinic, physician’s office, etc.), and any other unique circumstances. This information should not be used to replace, substitute for, or overrule a qualified medical professional’s judgment.

This website may contain third party materials and/or links to third party materials and third party websites for your information and convenience. Partners is not responsible for the availability, accuracy, or content of any of those third party materials or websites nor does it endorse them. Prior to accessing this information or these third party websites you may be asked to agree to additional terms and conditions provided by such third parties which govern access to and use of those websites or materials.
COVID-19 treatment: a primer

MGH-ID-CHANT Team
V 4.0 November 13, 2020
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>
</tr>
</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
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 only 1 FDA-approved treatment for COVID-19 (remdesivir)
- We may add treatment that has a goal 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
Remdesivir

- Remdesivir is an investigational drug that received emergency use authorization by the FDA on May 1, 2020 and was approved on October 22, 2020

- 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

- It should be avoided in patients with ALT >= 5x ULN

- eGFR < 30 is also a caution for remdesivir, which should be given when the benefits outweigh the risks

Remdesivir works like many antivirals that target the viral polymerase enzyme
Remdesivir (RDV) data as of October 30, 2020

• Results from randomized placebo-controlled trial from the NIH (ACTT-1) revealed:
  • Statistically significant reduction in time to recovery (10 days versus 15 days)
  • Non statistically significant reduction (HR 0.73) in 29-d mortality 11.4% (RDV) versus 15.2% (control)
  • Greatest benefit was seen in those on supplemental oxygen but not on high-flow, NIPPV, or mechanical ventilation
  • A large open-label (not blinded) randomized trial (SOLIDARITY) did not show a statistically significant difference in mortality; did not look at time to recovery (primary endpoint of ACTT-1); SOLIDARITY has not yet been peer-reviewed

ACTT-1 Trial, NEJM 2020 Solidarity Trial pre-print
Remdesivir talking points for patients

• Remdesivir directly slows down the part of the virus that makes new copies of itself
• It may be helpful to speed recovery
• You may be offered or may be receiving remdesivir, a drug approved by the FDA on October 22, 2020
• If receiving the medication, you are being monitored closely for side effects including checking your liver
• Some patients may experience an infusion reaction that passes
• We believe it works the best when patients are on oxygen, but may not have as much benefit before that or if patients are on a ventilator
Dexamethasone

• A large study indicated survival benefit of low dose dexamethasone for patients with severe or critical COVID-19, but no benefit in those not requiring oxygen support.

• Specifically, the mortality benefit was greater in a pre-specified subgroup of patients receiving mechanical ventilation (RR 0.64) than in those on supplemental oxygen (RR 0.82), with a non-statistically significant trend towards harm in those not on oxygen (RR 1.19).

• Given no benefit in those who are off oxygen, whether an oxygen requirement is new from a baseline requirement or due to other causes should be considered in the decision to start dexamethasone. Also, subgroup analysis suggests less benefit if administered ≤7 days after symptom onset.
Dexamethasone talking points for patients

• Dexamethasone is a cheap and widely available “steroid” that dampens the immune response to the virus that cause COVID-19

• It was shown to be helpful for those on oxygen and especially those who are on a ventilator

• You will receive up to 10 days of this medication, but if you are feeling better and can leave the hospital we can stop it earlier

• We will monitor you closely for side effects

• If your doctor has decided to give you another steroid, that’s fine as it is similar to dexamethasone
Monoclonal antibodies: talking points for patients

- Monoclonal antibodies against SARS-CoV-2 bind the virus and are part of a good immune response to COVID-19
- They may be more helpful earlier in disease (for example, before someone is hospitalized)
- Thus far, monoclonal antibodies are not helpful in hospitalized patients
- If offered under an emergency use authorization, permission or “assent” is required from yourself or your family
- If receiving the medication, you will be monitored closely
- Some patients may experience an infusion reaction that passes
What is emergency use authorization (EUA)?

• Under section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), the FDA Commissioner may allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by CBRN threat agents when there are no adequate, approved, and available alternatives.

• Until full FDA-approval, agents under EUA are considered investigational.

• Those receiving agents under EUA are not consenting to a study protocol but teams should obtain assent from patients or their families before writing the EPIC order.

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
Other medications

- We generally recommend 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 (a cohort study is reassuring regarding safety of NSAIDS in Covid-19)
  - 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 for treatment of Covid-19.
- There are no convincing data for hydroxychloroquine or azithromycin for COVID-19. Azithromycin may be used if there is another indication for its use.