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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

Symptom onset

Incubation Period | Acute Mild Phase * | ARDS/Pro-inflammatory Phase | Recovery
---|---|---|---
5.1 days (median) | 5-10 days | Days - weeks

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

Hallmarks: dyspnea, tachypnea, hypoxemia

Antibodies turn positive 6-12 days after symptom onset

SARS-CoV-2 Respiratory Viral RNA Load

Pan Lancet ID 2020 https://doi.org/10.1016/S1473-3099(20)30113-4
Zou NEJM 2020 DOI: 10.1056/NEJMc2001737
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 is 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. A clinical trial is currently available.
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)

ACTT-1 Trial, NEJM 2020 WHO Solidarity Trial Consortium
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.
Figure S5: Absolute effect of allocation to DEXAMETHASONE on 28-day mortality, by disease severity at randomisation.

**No oxygen**
- RR 1.22 (95% CI 0.93–1.61)
- p = 0.14

**Oxygen only**
- RR 0.80 (95% CI 0.70–0.92)
- p = 0.0921

**Ventilation or ECMO**
- RR 0.65 (95% CI 0.51–0.82)
- p = 0.0003

Number at risk:
- Dexamethasone: 501, 463, 420, 394, 383
- Usual care: 1034, 969, 890, 856, 832

Days since randomisation: 0, 7, 14, 21, 28
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
Tocilizumab

- Tocilizumab is a monoclonal antibody to the receptor for interleukin 6 (IL-6)
- IL-6 is a protein that the body makes when it is inflamed
- Tocilizumab does not block the virus directly
- Tocilizumab are likely safe, especially with short-term use
- Early studies did not show a benefit to tocilizumab, but these were largely conducted during a time before the standard of care included dexamethasone
- Recently, two studies (REMAP-CAP and RECOVERY) each demonstrated mortality benefit when used for a subset of patients, mostly those with rapidly increasing oxygen requirements, signs of inflammation (elevated CRP) and already on dexamethasone
Tocilizumab talking points for patients

• You may tocilizumab which is a drug used for other reasons and approved the FDA but is being used 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
• Tocilizumab both directly block the effects of this cytokine
• Two trials indicate that for certain patients, tocilizumab when added to dexamethasone may increase your chances of survival.
• You are being monitored closely for side effects, which may include increased risk of infection, elevated liver enzymes, neutropenia, and intestinal perforation.
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)
- 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

• There are **no data** regarding the safety or harm of NSAIDs, cohort studies are 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, azithromycin, or ivermectin** for COVID-19. Azithromycin may be used if there is another indication for its use.

• For outpatients with COVID-19, ACTIV-6 is a trial testing a variety of agents, including ivermectin. Additional information can be found at [https://combatcovid.hhs.gov/joinaclinicaltrial/activ-6](https://combatcovid.hhs.gov/joinaclinicaltrial/activ-6)