Category	Recommendations
Outpatient, asymptomatic	• Supportive care • Recommend against steroids
Outpatient, symptomatic	• Supportive care for most, consider clinical trials if eligible • High-risk for progression: Recommend outpatient therapy. See UCSF Adult Outpatient COVID-19 Treatment Guidance • Recommend against steroids
Inpatient, asymptomatic or mild symptoms and hospitalized for non-COVID-19 reason	• Supportive care, including prophylactic anticoagulation • Treat with one of the outpatient therapies if meets outpatient criteria • Recommend against steroids, therapeutic anticoagulation, or other anti-inflammatories
Inpatient, hospitalized for COVID-19 but does not require supplemental oxygen	• High-risk for progression or radiographic evidence of LRTI: Remdesivir x 5 days • Consider CCP if severe immunocompromise/not expected to mount an antibody response • Recommend against steroids or other anti-inflammatories • Prophylactic anticoagulation
Inpatient, Supplemental oxygen via nasal cannula	• Remdesivir x 5 days • Consider CCP if severe immunocompromise/not expected to mount an antibody response • Steroids if: Persistent hypoxia requiring ≥ 3-4L O_2 OR trajectory suggests increasing severity of disease • Consider therapeutic heparin-based anticoagulation if no contraindications
Inpatient, Requires supplemental oxygen via high-flow nasal cannula or non-invasive ventilation	• Remdesivir x 5 days • Steroids recommended • Consider adding baricitinib to steroids if rapid clinical worsening • Heparin-based *therapeutic* anticoagulation if < 20L HFNC and stable trajectory; otherwise, *prophylactic* anticoagulation • Consider CCP if severe immunocompromise/not expected to mount an antibody response
Inpatient, Requires mechanical ventilation or ECMO	• Remdesivir x 5 days • Steroids recommended • If baricitinib initiated before intubation, continue the course of medication • Alternative: Use tocilizumab if hospitalized < 3 days AND in ICU < 24 h AND rapidly progressing to mechanical ventilation or requiring mechanical ventilation. • Do not administer baricitinib and tocilizumab together • Consider CCP if severe immunocompromise/not expected to mount an antibody response • Recommend against therapeutic anticoagulation; prophylactic anticoagulation as indicated

Table 1. Diagnostic testing for patients with confirmed or suspected COVID

Testing for COVID-19.	
Initial testing for symptomatic patients: **COVID-19 PCR via** Nasopharyngeal (NP) +/- Oropharyngeal (OP), Mid-Turbinate (MNT) +/- OP, or Anterior Nares (AN) +/- OP (note that flu/RSV and RVP cannot be performed on AN samples)	**Repeat PCR testing:** If negative initial PCR and very high suspicion: ○ Tracheal aspirate COVID-19 PCR in mechanically ventilated patients ○ Repeat NP or MNT + OP testing if not mechanically ventilated Certain COVID-19 confirmed patients may require additional testing for disposition; consult ID to discuss next steps Retesting of previously negatively tested patients should be done if: ○ New compatible symptoms ○ Exposure investigation ○ Planned or continuous aerosol-generating procedure (every 7 days) ○ Shared room (Monday and Thursday)
Serologic testing, clinical indications: ○ Confirmation of infection if high clinical suspicion, negative PCR testing, and symptoms > 7 days ○ Documentation of serological response prior to convalescent plasma donation ○ Utility for determining immunity uncertain	
Laboratory testing	
On admission *All patients*[1]*:* ○ CBC with differential, BMP, LFTs, coagulation studies ○ Consider SARS-CoV-2-Ab IgG Nucleocapsid Protein if planning CCP	*Routine monitoring*: If receiving medications to treat COVID-19, obtain daily CBC with differential, BMP, Mg Trend LFTs Q48h-72h if abnormal at baseline (> 2 x ULN) or receiving remdesivir therapy

○ Send RVP if during flu season (declared by HEIP and executive leadership based on Bay Area flu incidence) *If clinically indicated:* ○ Procalcitonin, troponin, BNP, lactate, ABG ○ If concern for bacterial infection (prior to starting empirical antibiotics): blood cultures (2 sets), sputum bacterial culture ○ Hepatitis B and C serologies if elevated liver biochemistries ○ *Consider* to estimate risk for severe disease: fibrin d-dimer, CRP, LDH and CPK.	*If clinical deterioration*: ○ Repeat sputum and blood cultures (tracheal aspirate culture if intubated)
Do not obtain unless clinical suspicion for a specific diagnosis (e.g. HLH) ○ Ferritin, soluble IL-2-receptor-alpha, NK cell activity **Do not obtain:** ○ IL-6 levels	
Imaging	
Chest radiograph: ○ Baseline AP CXR on admission ○ Monitoring for complications (pneumothorax, atelectasis) at interval deemed appropriate by clinical team	**Chest CT:** ○ Limited role in diagnosis of COVID-19 (PCR test of choice) ○ Primary role is evaluation of superimposed processes such as pulmonary embolism or aortic dissection.

Table 2. Therapeutics

Therapies	
○ Multiple clinical trials continue to enroll inpatients and outpatients ○ Clinical trial teams will screen inpatients for eligibility and offer enrollment ○ Experimental therapeutics should only be offered in the context of a clinical trial	
Antibiotics	○ Bacterial co-infection on initial presentation to the hospital for COVID-19 is uncommon. Use antibacterials sparingly in this population, and if started, deescalate rapidly for negative cultures.

	○ For patients admitted with severe and critical COVID-19, hospital-acquired infections may occur with both bacterial and fungal pathogens. Decisions to initiate therapy should be based on clinical data.
Baricitinib or tocilizumab	Recent studies of JAK inhbitors, including baricitinib, have demonstrated reduced disease progression and decreased mortality in patients requiring significant oxygen support. Other studies of IL-6 inhibitors, including tocilizumab, show improved clinical outcomes and decreased mortality, especially in recently admitted patients in the ICU requiring intubation. Updated NIH guidance recommends "using either **baricitinib (BIIa)** or **tocilizumab (BIIa)** (listed alphabetically) in combination with **dexamethasone** alone or **dexamethasone plus remdesivir** for the treatment of COVID-19 in hospitalized patients on high-flow oxygen or noninvasive ventilation who have evidence of clinical progression or increased markers of inflammation." The NIH Panel could not reach consensus on a recommendation for use of either medication for patients with signs of systemic inflammation and rapidly increasing oxygen needs while on steroids but not requiring non-invasive ventilation or high flow oxygen. The NIH panel did not comment on their prior recommendation to use tocilizumab in recently admitted patients requiring ICU care < 24h and mechanical ventilation. In consideration of these NIH recommendations, and new baricitinib clinical trial data, **our updated guidance:** • Consider <u>baricitinib</u> if the following criteria are met: ○ Use with steroids (preferred, meets all below): ▪ Severe or critical disease and meets criteria for steroids ▪ Escalating oxygen via nasal cannula, high flow oxygen, or non-invasive ventilation ○ Use in place of steroids: ▪ Meets criteria for steroids AND ▪ Has a contraindication to steroids • <u>Baricitinab dosing:</u> ○ 4 mg PO once daily up to 14 days while in the hospital

	○ Adjust dosing for renal failure as follows: ▪ ▪ CrCl 30-59 mL/min: 2 mg PO once daily ▪ ▪ CrCl 15-29 mL/min: 1 mg PO once daily ○ Contraindications: ▪ CrCl < 15 mL/min ▪ Use with caution in immunocompromised patients ▪ Discontinue if absolute lymphocyte count < 200 cells/ml or ANC < 500 cells/ml. Can restart once above these thresholds. ▪ Interrupt treatment if drug-induced liver injury is suspected or if ALT and/or AST rises to > 10x upper limit of normal • Use tocilizumab as an alternative to baricitinib if hospitalized < 3 days AND in ICU < 24 hours AND rapid disease progression with imminent requirement for mechanical ventilation or already requiring mechanical ventilation. ○ Administer with steroids. • Tocilizumab dosing: 8 mg/kg IV x 1 dose (maximum dose: 800 mg) ○ Contraindications: ▪ Serious concomitant infection ▪ Use with caution in immunocompromised patients, especially if recent immunomodulating drugs ▪ Lab abnormalities: ANC < 500, platelets < 50, ALT > 5x ULN ○ Do not administer baricitinib and tocilizumab together ○ ID consultation recommended for use of both baricitinib and tocilizumab. ○ Avoid use of these agents in pregnancy given lack of safety data. Both agents may be used during lactation. If baricitinib is administered, breastmilk should be discarded until 3 days after last dose. Consult with OB and pharmacy prior to administration. ○ Both agents require ID approval for this indication
Convalescent plasma	○ High-titer units available via EUA**.**

	○ Outside of clinical trial, may consider for use if: Severe immunocompromise not expected to mount an antibody response (e.g. recent solid organ transplant or stem cell transplant) ○ Use caution if concern for volume overload (e.g. severe liver disease, heart failure, renal failure not yet on renal replacement) ○ Process: ○ Requires ID approval ○ Give EUA Fact Sheet to patient or surrogate and inform them that CCP is investigational and discuss potential risks (transfusion reaction) / benefits (unclear) ○ Get / ensure up to date Type and Screen ○ Obtain standard blood product consent form ○ Once patient agrees, places order (under "IP Adult Standard Transfusion Orders," selection "COVID convalescent plasma")
Monclonal antibodies	Currently on hold as of 11/17/2022 due to predicted resistance of circulating strains to currently available antibodies
Remdesivir	Initial data suggest some benefit in time to recovery and possibly in mortality. FDA approved ○ Treatment should be administered to hospitalized patients with evidence of lower respiratory tract infection (e.g. hypoxia, abnormal chest radiograph) ○ Dosing: ○ Outpatient or admitted for other diagnosis: 200mg IV x 1, then 100mg IV q24h for 2 additional days ○ Admitted for COVID-19: 200mg IV x 1, then 100mg IV q24h for 4 additional days ○ Vehicle contains cyclodextrin, which can accumulate in renal failure. Not well studied in renal replacement therapy (including intermittent hemodialysis), though likely to be safe given short duration of therapy. Dose adjustment is not required. ○ Contraindications: ○ ALT/AST > 10 times the upper limit of normal ○ Allergy ○ Requires ID approval (initial overnight dose is unrestricted)
Steroids	Initial data suggests mortality benefit in those with severe or critical disease. No benefit (and trend towards harm) seen in those who do not require supplemental oxygen. Off-label use.

	○ Dosing: Dexamethasone 6 mg IV or PO qday (or equivalent) up to 10 days while in the hospital. Administer PO if able to take oral medication. ○ Populations: ○ Patients undergoing mechanical ventilation, non-invasive ventilation, or high-flow nasal cannula: Most patients should be treated with steroids ○ Patients on nasal cannula: Consider steroids in those with persistently low oxygen saturation and requiring substantial supplemental oxygen (e.g. ≥ 3-4L O2) or whose trajectory suggests increasing severity of disease ○ Contraindications: ○ Patients who do not require supplemental oxygen should not get steroids for the indication of COVID-19 Factors to consider in determination of whether to withhold (or stop) steroids: • Uncontrolled invasive fungal infections • Uncontrolled hyperglycemia • Existing delirium • Other immunosuppressive medications • Pregnancy (dexamethasone crosses the placenta and should be discussed with OB/Maternal-Fetal Medicine before administration) *Consult ID for patients with any of the above factors to discuss relative risk/benefit of steroid administration*
Tocilizumab	See "baricitinib and tocilizumab" section
Medications to avoid	
Other antiviral and immunolomodulatory agents (e.g. hydroxychloroquine, ivermectin, fluvoxamine)	Do not give other pharmaceutical treatments specifically for COVID-19 unless part of a clinical trial
Anticoagulation	

Data support a hypercoaguable state in COVID-19 infection. Results from several large studies comparing prophylactic with therapeutic anticoagulation suggest benefit in patients with moderate but not severe infection. Patients hospitalized for COVID-19 and requiring supplemental oxygen but not high-flow nasal cannula or ventilatatory support experience higher odds of surviving to discharge without requiring organ support with therapeutic compared to prophylactic heparin. Overall survival to discharge was not different between groups. Severely ill patients do not benefit from therapeutic anticoagulation and may be harmed by bleeding risks.

- **Prophylactic heparin-based anticoagulation** (e.g. sub-cutaneous heparin or enoxaparin):
  - Dosing: Standard venous thromboembolism (VTE) prophylaxis dosing should be used
  - Population:
    - No supplemental oxygen need or hospitalization for reasons other than COVID-19
    - Requires supplemental oxygen but patient or provider preference for prophylactic rather than therapeutic dosing
    - Requires NIPPV or oxygen therapy >20L
    - Requiring ICU level care
  - Contraindications: Any contraindication to heparin or prophylactic anticoagulation, such as active CNS bleed, severe thrombocytopenia with platelet count < 25,000, history of heparin-induced thrombocytopenia

- **Therapeutic heparin-based anticoagulation**:
  - Dosing: Standard VTE treatment dosing of heparin-based anticoagulation. Continue for no more than 14 days and should be discontinued on discharge. Enoxaparin is preferable to unfractionated heparin unless CrCl < 15 or other contraindication.
    - Decreasing to prophylactic dose may be considered with resolving clinical course (e.g. discontinuation of oxygen) or if clinical severity increases to ICU level support or oxygen >20L at the discretion of the clinical team given lack of clear data in this area
    - For patients already on chronic full dose anticoagulation (e.g. DOAC, warfarin), this may be continued instead of heparin-based anticoagulation
  - Population:
    - Consider in non-critically ill patients requiring supplemental oxygen or stable/improving HFNC < 20L. This approach may decrease need for ICU level care and organ support for COVID-19.

- In weighing decision to initiate therapeutic versus prophylactic anticoagulation, must weigh potential benefits with risks and patient preference.
  - Potential benefits: decreased need for organ support but no difference in survival
  - Potential risks: bleeding complications
- Contraindications: Any contraindication to heparin or therapeutic anticoagulation, such as dual antiplatelet therapy, major bleeding with the last 30 days, known acquired or inherited bleeding disorder, history of heparin induced thrombocytopenia, recent ischemic stroke, platelet count < 50 x 10^9/L, Hemoglobin < 8 g/dL, or clinical discretion of the treating physician

Immunosuppression

- In immunosuppressed patients without COVID-19, do not make anticipatory adjustment to current immunosuppressive drugs or dosages
- In immunosuppressed patients with COVID-19, consider reducing levels of immunosuppression if possible

Other

- **Renin-angiotensin system (RAS) blockers**
  - Theoretical concerns have been raised as some RAS blockers may increase expression of ACE2, which may facilitate viral entry into cells. However, currently there is not clinical or epidemiological data to support this concern. Patients who routinely take ACE inhibitors or ARB medications should generally continue these medications.
- **Nonsteroidal anti-inflammatory drugs**
  - Concerns have been raised that NSAIDs may worsen COVID-19 disease. However, to date, there is no scientific evidence connecting the use of NSAIDS with worsening COVID-19 symptoms or outcomes.

Table 3: Critical Care

Respiratory and Ventilator Management

Only essential providers in the room during intubation or other aerosol generating procedures

Nebulizer therapy:

- Nebulizer therapy is an aerosol generating procedure and should be avoided except:
  - ICU-level care due to respiratory status
  - Requiring high-flow nasal oxygen or non-rebreather mask
  - Inability to follow commands (altered mental status, severe cognitive impairment)

- Mechanically ventilated and can be delivered in-line with circuit.

Non-invasive respiratory support:

- High flow nasal oxygen (HFNO) should be considered for use in hypoxemic patients but caution with higher flows (e.g. >25 LPM) in order to avoid emergent intubation. Close monitoring of respiratory status is essential.
- Non-invasive ventilation (NIV, e.g CPAP or BiPAP) should only be used in selected patients with respiratory failure or known obstructive sleep apnea
- Both HFNO and NIV are aerosol generating procedures and require airborne precautions
- Patients receiving either HFNO or NIV should be cared for in a monitored setting by personnel capable of performing endotracheal intubation

Intubation:

- Emergent intubations are to be avoided given the prolonged time to apply PPE and increased risk of infection to the person performing the intubation
- Only experienced providers should perform intubation
- Consider video laryngoscopy as preferential airway equipment
- Once intubated, minimize circuit disconnects and use in-line suction

Mechanical Ventilation and Advanced Respiratory Care:

- Lung protective ventilation is the mainstay of care: preferred mode is volume controlled ventilation with low tidal volume (6 mL/kg predicted bodyweight) with a plateau airway pressure of less than 30 cm H2O.
- For severe hypoxemia (P/F ratio < 150) consider:
  - Moderate-high PEEP
  - Recruitment maneuvers (monitor hemodynamics and discontinue if patient develops hypotension or no improvement in driving pressure or oxygenation)
  - Deep sedation +/- neuromuscular blockade, especially with ventilator asynchrony
  - Early use of manual proning

Extracorporeal Membrane Oxygenation (ECMO) Considerations

ECMO (VA or VV, as appropriate) will be considered per criteria established by Critical Care Medicine and Cardiac Surgery

Continuous Renal Replacement Therapy (CRRT)

○ For patients with acute kidney injury (AKI), consider delaying CRRT until significant metabolic complications arise (K > 5.5 mmol/L) or until significant positive fluid balance despite high-dose diuretics or unable to achieve lung protective ventilation due to severe metabolic acidosis ○ For ESRD patients, CRRT should be used to avoid markedly positive fluid balance, which may exacerbate hypoxemia

Table 4: Palliative Care

Palliative Care (PC) best practices
For primary teams: ○ Perform a Goals of Care discussion within 48hrs of admission and offer age- and comorbidity-specific prognostic information ○ Use the comfort care order set for actively dying patients (consult PCS only if there are questions or additional support is needed)
Indications for Palliative Care Consultation unique to patients with COVID-19
○ Consider for patients requiring ICU-level care ○ Emotional, spiritual and symptomatic support at the end of life for patient/family ○ Ethical decision making
Caring for the Caregiver
○ The Caring for the Caregiver Program is dedicated to providing support to faculty, staff and trainees experiencing emotional distress related to the clinical care of patients ○ Please contact **caringforthecaregiver@ucsf.edu** anytime to request support for yourself or a peer (can also coordinate group debriefings)

Table 5: Discontinuation of isolation and discharge considerations

Discontinuation of Isolation at UCSF Health
See COVID-19 Guidelines for Discontinuing of Isolation
Discharge considerations
○ Discharge coordination for hospitalized patients with COVID-19 requires advanced planning and close coordination between multiple disciplines in the hospital including clinicians, infection control, and case management, particularly for discharge to congregate settings

- Case Management notifies local DPH via CMR Form Submission for new COVID + admissions
- Case Management cooridnates with local DPH for discharge clearance for some SNF or other facility placements
- Case Management/Social work will coordinate COVID isolation transport when necesssary
- Explicit guidance and return precautions for evaluation of concerning symptoms after discharge must be provided (utilize prepared communications tools with anticipatory guidance)
- Inpatient discharge dot-phrases:
  - .COVIDPOSINPTDCED
  - .COVIDPOSINPTDCEDES (Spanish)
- Outpatient discharge dot-phrase:
  - .COVIDDISCHARGEADULT

Self-discharge:

- <u>All Patients</u>
  - Provider to call SF DPH AMA line at 415-608-1515
  - CM to provide local DPH isolation guidleines
- <u>Homeless patients</u>
  - Email DPH AMA recovery at covid19AMArecovery@sfdph.org (24/7, 7 days a week) and/or call 415-608-1515 (M-F 8am-8PM)
  - Include information:
    - name
    - date of birth
    - time they departed
    - whether they are a PUI or Covid Positive
    - Information about where they may have gone/phone number
  - DPH contact: Sarah Strieff RN 415-238-1485 or sarah.strieff@sfdph.org

Discharge to Skilled Nursing Facilities

- Case Management will coordinate with local DPH and/or admission staff to determine their ability to accept COVID patients needing isolation.
- Some SNFs are given blanket clearance from DPH to admit COVID patient

Many SNFs requires COVID isolation period of 10 vs 20 days to be completed as well as afebrile x 24 hours prior to admission

Discharge to Group Settings

- If the patient has the ability to isolate after discharge, they are able to return to RCFE/Group setting.

Reviewed by representatives from:
-Care Delivery Committee
-Hospital Medicine
-Critical Care Medicine
-Infectious Diseases
-Pharmacy
-Nephrology
-Case Management

References:

1. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of COVID-19—final report. N Engl J Med. 2020. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32445440.
2. Bhimraj A, Morgan RL, Shumaker AH, Lavergne V, Baden L, Cheng VC, Edwards KM, Gandhi R, Gallagher J, Muller WJ, O'Horo JC, Shoham S, Murad MH, Mustafa RA, Sultan S, Falck-Ytter Y. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19. Infectious Diseases Society of America 2021; Version 4.1.0. Available at https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/. Accessed 3.16.2021.
3. Cavalcanti AB, Zampieri FG, Rosa RG, et al. Hydroxychloroquine with or without azithromycin in mild-to-moderate COVID-19. N Engl J Med. 2020; Published online ahead of print. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32706953.
4. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines.nih.gov/. Accessed 9.8.2021.
5. Food and Drug Administration. Frequently Asked Questions on the Emergency Use Authorization of Baricitinib for Treatment of COVID-19. https://www.fda.gov/media/143825/download.
6. Food and Drug Administration. Fact Sheet for Health Care Providers Emergency Use Authorization of COVID-19 Convalescent Plasma for Treatment of Hospitalized Patients with COVID-19. https://www.fda.gov/media/141478/download. Accessed 3.16.2021.
7. Goldman JD, Lye DCB, Hui DS, et al. Remdesivir for 5 or 10 days in patients with severe COVID-19. N Engl J Med. 2020. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32459919.

8. Gottlieb RL, Nirula A, Chen P, et al. Effect of Bamlanivimab as Monotherapy or in Combination With Etesevimab on Viral Load in Patients With Mild to Moderate COVID-19. JAMA 2021: doi:10.1001/jama.2021.0202.
9. Gottlieb RL, Vaca CE, Paredes R, et al. Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients. NEJM 2021: DOI: 10.1056/NEJMoa2116846
10. Guimaraes PO, Quirk D, Furtado RH, et al. N Engl J Med 2021. DOI: 10.1056/NEJMoa2101643
11. Hermine O, Mariette X, Tharaux PL, et al. Effect of tocilizumab vs usual care in adults hospitalized with COVID-19 and moderate or severe pneumonia: a randomized clinical trial. JAMA Intern Med. 2021;181(1):32-40. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33080017.
12. Joyner MJ, Carter RE, Senefeld JW, et al. Convalescent Plasma Antibody Levels and the Risk of Death from Covid-19. N Engl J Med 2021.
13. Kalil AC, Patterson TF, Mehta AK, et al.; ACTT-2 Study Group Members. Baricitinib plus Remdesivir for Hospitalized Adults with Covid-19. N Engl J Med. 2021 Mar 4;384(9):795-807. doi: 10.1056/NEJMoa2031994. Epub 2020 Dec 11. PMID: 33306283; PMCID: PMC7745180.
14. Libster R, Pérez Marc G, Wappner D, et al. Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults. N Engl J Med 2021; 384:610.
15. Marconi VC, Ramanan AV, de Bono S, et al. Efficacy and safety of baricitinib for the treatment of hospitalised adults with COVID-19 (COV-BARRIER): a randomised, double-blind, parallel-group, placebo-controlled phase 3 trial. Lancet Respir Med 2021. Published online September 1 2021.
16. RECOVERY Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with COVID-19 - preliminary report. *N Engl J Med*. 2020. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32678530.
17. RECOVERY Collaborative Group, Horby PW, Pessoa-Amorim G, et al. Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): preliminary results of a randomised, controlled, open-label, platform trial. medRxiv. 2021;preprint. Available at: https://www.medrxiv.org/content/10.1101/2021.02.11.21249258v1.
18. REMAP-CAP Investigators, Gordon AC, Mouncey PR, et al. Interleukin-6 receptor antagonists in critically ill patients with COVID-19. N Engl J Med. 2021. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33631065.
19. Salama C, Han J, Yau L, et al. Tocilizumab in patients hospitalized with COVID-19 pneumonia. N Engl J Med. 2021;384(1):20-30. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33332779.
20. Salvarani C, Dolci G, Massari M, et al. Effect of tocilizumab vs standard care on clinical worsening in patients hospitalized with COVID-19 pneumonia: a randomized clinical trial. JAMA Intern Med. 2021;181(1):24-31. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33080005.

21. Self WH, Semler MW, Leither LM, et al. Effect of Hydroxychloroquine on Clinical Status at 14 Days in Hospitalized Patients With COVID-19: A Randomized Clinical Trial. JAMA. 2020;324(21):2165–2176. doi:10.1001/jama.2020.22240
22. Spinner CD, Gottlieb RL, Criner GJ, et al. Effect of remdesivir vs standard care on clinical status at 11 days in patients with moderate COVID-19: a randomized clinical trial. JAMA. 2020;324(11):1048-1057. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32821939.
23. Stone JH, Frigault MJ, Serling-Boyd NJ, et al. Efficacy of tocilizumab in patients hospitalized with COVID-19. N Engl J Med. 2020;383(24):2333-2344. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33085857.
24. The ATTACC, ACTIV-4a, and REMAP-CAP Investigators. Therapeutic Anticoagulation with Heparin in Noncritically Ill Patients with Covid-19. N Engl J Med 2021; 385:790-802. DOI: 10.1056/NEJMoa2105911
25. The ATTACC, ACTIV-4a, and REMAP-CAP Investigators. Therapeutic Anticoagulation with Heparin in Critically Ill Patients with Covid-19. N Engl J Med 2021; 385:777-789. DOI: 10.1056/NEJMoa2103417
26. Wang Y, Zhang D, Du G, et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. Lancet. 2020;395(10236):1569-1578. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32423584.
27. Weinrich DM, Sivapalasingam S, Norton, T, et al. REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19. NEJM 2021; 384:238-251. DOI: 10.1056/NEJMoa2035002