V10 rev 9/23/20 (orig 3/26/20)
Contact Colby Miller, PharmD for more info or comments. Colby.A.Miller@MedStar.net

Treatment Guidance for Covid-19 Infections (therapeutic options are not mandatory, evidence is evolving)

Pt admitted for COVID-19+

Significant hypoxemia treated with supplemental oxygen

Yes

No

Supportive Care

Consider remdesivir – Data for benefit is most robust in patients who are on supplemental oxygen who have inadequate improvement in respiratory function but do not require high-flow oxygen, mechanical ventilation, or ECMO. Additional data is needed to establish the benefit of remdesivir in those requiring either no oxygen support or requiring mechanical ventilation +/- ECMO.

Patient must meet all the following criteria to receive remdesivir:

- eGFR ≥30, not on renal replacement therapy
- AST/ALT < 5x ULN
- Reasonable expectation of survival
- Lack of a medical condition(s) that will result in near-term mortality (life expectancy under 6 months) even with aggressive therapy
- Lack of advanced and irreversible neurologic event or condition such that patient will be unable to later perceive the benefits of having received treatment

Remdesivir 5-day regimen (or until discharge, whichever is sooner)

- *Requires ID (if site availability) or Critical Care and Pharmacy approval*
- *Requires patient informed consent (see link to patient info sheet in Appendix 1)*
- *There is insufficient data on extension of treatment in patients who have not improved after 5 days. Some experts extend remdesivir up to 10 days in these cases.*

COVID-19 Symptoms >7 days?*

Yes

Consider dexamethasone 6 mg PO/NG/IV daily x 10 days (or until discharge, if sooner)

Pregnant/lactating women: Prednisolone 40 mg PO daily or hydrocortisone 80 mg IV BID

See appendix 1 for dosing and alternative corticosteroids.

**If duration of symptoms is unknown, may consider dexamethasone if deemed clinically warranted. There is a lack of data on outcomes of dexamethasone in mechanically ventilated patients with duration of COVID-19 symptoms <7 days.*

Treatments in Review (benefit and risks may not yet be proven in COVID-19)

Dexamethasone – findings in the Recovery Trial demonstrate improved mortality in patients receiving oxygen or on the ventilator. Note: in those not receiving supplemental oxygen, dexamethasone may have been associated with harm.

Remdesivir – antiviral with FDA emergency use authorization for COVID-19+ hospitalized patients

Convalescent plasma – the FDA has approved use under an emergency use authorization. Please see table below and separate MedStar guidance resources for additional information.

Tocilizumab – the COVACTA trial demonstrated no clinical or mortality improvement in patients with severe COVID-19 pneumonia. Additional trials are in progress. Consider use only within a clinical trial.

Appendices:

Appendix 1: Brief overview of agents			
Current literature is evolving, and no medication therapies have conclusively demonstrated improved outcomes in Covid-19 patients. For an up-to-date literature evaluation of therapies, click here. For all COVID-19 clinical trials in progress, click here. If, on a case by case basis, a clinical decision is made to utilize a therapy outside of a clinical trial, select dosing regimens used in COVID-19 are listed below.			
Agent	**Dosing / Administration**	**Safety**	**Notes**
Remdesivir MOA: RNA dependent RNA polymerase inhibitor	Adults and children ≥40 kg: 200 mg IV x 1 dose, then 100 mg IV daily Children between 3.5 kg and <40 kg: 5 mg/kg IV x 1 dose, then 2.5 mg/kg IV q24h Infuse dose over 30-120 minutes	Nausea, vomiting, elevated aminotransferase, headache, constipation, phlebitis, pain in extremity Avoid in patients with ALT ≥5 x upper limit of normal (ULN) Avoid in patients with GFR <30 mL/min. If eGFR falls below 30 during treatment with RDV, weight the potential risks and benefits of continuing therapy Discontinue if: • ALT > 5 x ULN • ALT ↑with s/s liver inflammation or ↑conjugated Bili, alk phos, or INR Drug interactions are possible (not studied in humans yet). Remdesivir is a substrate for CYP2C8, CYP2D6, CYP3A4, OATP1B1, and P-gp transporters. It inhibits CYP3A4, OATP1B1, OATP1B3, BSEP, MRP4, and NTCP.	On 8/29, the FDA expanded the EUA to include all hospitalized suspected or positive COVID-19 patients. However, currently, evidence is insufficient to support use beyond the patients with an SPO2>94% not on oxygen or in those requiring mechanical ventilation +/- ECMO. If more robust data becomes available to support the use of remdesivir in these populations, the MedStar guidance will be updated to reflect this. Additional Resources (click to access): NIH Remdesivir Guidance 7-24-20 Patient/Caregiver Fact Sheet for Remdesivir Patient/Caregiver Fact Sheet for Remdesivir in Spanish Provider Fact Sheet for Remdesivir Report any serious safety events via: FDA MedWatch Adverse Event Reporting - electronic Or FDA MedWatch Downloadable Form

Tocilizumab (Actemra®) MOA: Monoclonal antibody to IL6 receptor/ treats cytokine release syndrome	8 mg/kg (max 800 mg) IV x 1 dose, repeat in 12 hours if no improvement or worsened. See clinical trials (in the reference section) for additional dosing regimens and inclusion/exclusion criteria.	ALT elevations GI perforation, anemia, hepatitis, neutropenia, infusion reactions	Given the lack of benefit demonstrated in the COVACTA study, use should be limited to clinical trial only. Not antiviral Avoid in pregnancy/breast feeding Baseline T-SPOT, and inflammatory markers (e.g. CRP, Ferritin, ESR, fibrinogen, D-dimer) (do not delay therapy) and as needed based on clinical condition. IL-6 levels may be sent but should NOT guide decision to administer tocilizumab due to delay in result turn-around time.
Sarilumab (Kefzara®) MOA: Monoclonal antibody to IL6 receptor	Randomized to 200 mg, 400 mg, or placebo IV x1 dose	Neutropenia, elevated ALT, GI perforation, infusion reactions	NOTE: US study in mechanically ventilated patients halted due to lack of benefit and increased side effects. No positive data exists currently to support use outside of a clinical trial.
Convalescent plasma (cFFP) MOA: confers passive immunity by providing antibodies from previously exposed COVID-19 patients. This approach has been effective in treating other viral disease (eg, hepatitis A and B, mumps, polio, measles, SARS-CoV-1, et al). The antibodies inactivate the virus. Several case series suggest possibly shorter duration of illness without adverse effects. Based on use in other viral diseases, it is felt to be most effective when used earlier in the course of disease.		Risks include pathogen transmission, infusion reactions, transfusion-related acute lung injury (all rare).	On Aug 23, 2020, the U.S. FDA approved the use of COVID-19 Convalescent Plasma (CCP) under an Emergency Use Authorization (EAU) as passive immune therapy for the treatment of hospitalized patients with COVID-19. Limited data suggests that treatment early (<3 days) in the course of disease (prior to intubation) would be expected to have more benefit. However, adequate and well-controlled randomized trials have not been performed. In addition, there is some evidence to suggest that CCP with higher antibody content may be more likely to be effective, at this time most of the available CCP does not have a quantitative antibody titer. Should clinicians decide to administer CCP, the following guidance is suggested:

			1. CCP should be reserved for hospitalized patients who require supplemental oxygenation 2. CCP should be dosed as one CCP unit (about 200 mL), with additional dosing based on the physician's medical judgement (for example, response to CCP or weight-based dosing) 3. Patients with impaired cardiac function/heart failure or ESRD may require a smaller volume or more prolonged transfusion times Refer to Starport for these additional documents: **Interim 90-day Guidance for Clinicians on the Use of COVID-19 Convalescent Plasma, Fact Sheet for Patients – CCP, and Fact Sheet for Providers – CCP – EUA interim guidance.** Providers/residents are encouraged to provide patients who are being discharged after recovery with information about how to contact the Red Cross for the donation of convalescent plasma. Click here to access the Red Cross information for convalescent plasma donation.
Dexamethasone and other corticosteroids Corticosteroids may help suppress the cytokine storm in COVID-19 ARDS.	**Dexamethasone (based on the Recovery Trial)** Adults (non-pregnant/lactating): 6 mg PO/NG/IV daily x 10 days (discontinue on discharge, if sooner) Children: 150 mcg/kg (as base) PO/NG/IV daily (max: 6 mg) (discontinue on discharge, if sooner) Pregnant/lactating women: Prednisolone 40 mg PO daily or hydrocortisone 80 mg IV BID should be used instead of dexamethasone.	Dexamethasone, methylprednisolone, and prednisone cross the placenta and are present in breast milk. Hydrocortisone sodium succinate is enzymatically inactivated in the placenta, thus limiting fetal exposure. Avoid formulations containing benzyl alcohol. Hydrocortisone is present in breast milk. According to Bae et al, the amount of prednisolone in breast milk is minimal and based on the half-life of cortisol,	The Recovery Trial demonstrated dexamethasone improved mortality in patients receiving oxygen or on the ventilator. 28-day mortality in patients receiving dexamethasone was 21.6% vs 24.6% in those receiving usual care. This reduction in mortality was seen in those with symptoms for more than 7 days. Those receiving mechanical ventilation had a 35% decrease in 28-day mortality and those receiving oxygen without mechanical ventilation had a 20% decrease. Note: no benefit was seen with dexamethasone in those not

	Alternative corticosteroids if dexamethasone is unavailable (note: these were not included in the Recovery Trial) Adults: Prednisone 40 mg PO daily Methylprednisolone 32 mg PO/IV daily (or in divided doses) Hydrocortisone: clinical trials in COVID-19 included 50 mg IV q6h x 7 days or 200 mg/day continuous infusion, however, the optimal dose has not been established. The Recovery Trial used 80 mg IV BID in pregnant COVID-19 patients. Pediatric: Consult appropriate references for dosing of alternative corticosteroids.	exposure to corticosteroids can be avoided by waiting 4 hours after the dose to breastfeed. All patients: monitor for hyperglycemia, hypertension, immunosuppression	receiving any respiratory support and dexamethasone may have been associated with harm in those patients.
Transplant patients: Consult the transplant service (nephrology or surgery) immediately. Do not make empiric adjustments to immunosuppression without guidance from these services. Sites without transplant services should contact the patient's outpatient transplant provider immediately for guidance on immunosuppressant management.			

Appendix 2: ACE inhibitors (angiotensin converting enzyme inhibitors) and ARBs (angiotensin-receptor blockers)
• It is strongly recommended that patients on existing treatment **should be continued on their ACE inhibitor and ARB therapy** • Currently, there is no scientific or clinical evidence that taking ACE inhibitors or ARBs increases the risk of acquiring COVID-19 or that use may increase the severity of illness for those acquiring the infections. • Patients should NOT be started on an ACE inhibitor or an ARB in the setting of COVID-19 treatment.

Appendix 3: Agents with limited data for COVID-19 therapy	
Azithromycin (Zithromax®)	Azithromycin demonstrates some antiviral activity in vitro. Limited clinical experience in COVID-19 shows mixed results. Concerns have been raised regarding drug-drug interactions (especially QTc prolongation with hydroxychloroquine or chloroquine). Note: a patient who has community acquired pneumonia (CAP) may be receiving azithromycin as part of a CAP regimen (e.g., with ceftriaxone).
Hydroxychloroquine (Plaquenil®) **Chloroquine phosphate** (Aralen®)	While these agents demonstrate antiviral activity in vitro, they were not shown to be of benefit in treatment of COVID-19 in hospitalized patients and may increase the risk of QTc prolongation.
Lopinavir/ritonavir (Kaletra®)	Lopinavir inhibits the protease activity of coronavirus in SARS. Limited clinical experience in COVID-19 shows mixed results. Efficacy has not been definitively established and clinical trials are on-going. Due to risk of adverse events and drug-drug interactions, along with a lack of robust data in COVID-19 at present time, not currently recommended.
Darunavir/cobicistat (Prezcobix®)	Currently being evaluated in a clinical trial but no in vitro or in vivo data exist to support use at this time.
Oseltamivir (Tamiflu®)	SARS-CoV-2, the virus that causes COVID-19, does not use neuraminidase as part of the viral replication cycle so oseltamivir is unlikely to be of therapeutic value, and supplies of the drug should be preserved for patients with

	influenza.
IVIG	IVIG remains on critical national shortage. The benefit in patient with COVID-19 is unclear.
Ribavirin	Role unclear, doses required for optimal antiviral activity often exceed limit of patient tolerability. Risk of toxicity likely outweighs potential clinical benefit.
Nitazoxanide	Displays inhibitory activity against the virus in vitro however no clinical data in humans exists.
IV Vitamin C (ascorbic acid) and thiamine	Recent data shows these agents combined with hydrocortisone did not lead to more rapid resolution of septic shock compared to intravenous hydrocortisone alone. It is unclear if these agents have any impact on viral illnesses.

Appendix 4: References

- Chen N et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study.' Lancet; 395(10223):507- 513.
- Colson P, Rolan JM, Lagier JC, Brouqui, Raoult D. Chloroquine and hydroxychloroquine as available weapons to fight COVID-19. Int J Antimicrob Agent 2020 (epub ahead of print).
- De Wit, E et al. Prophylactic and therapeutic remdesivir (GS-5734) treatment in the rhesus macaque model of MERS-CoV infection. Proceeding of the National Academy of Sciences of the United States of America. First published February 13, 2020 https://doi.org/10.1073/pnas.1922083117.
- Lai C-C, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. Int J Antimicr Agents 2020; In press. https://doi.org/10.1016/j.ijantimicag.2020.105924
- Liverpool COVID-19 Crush/Chew/Liquid Guide COVID Swallowing_2020_Mar13 (1).pdf. Accessed March 16, 2020. https://www.covid19-druginteractions.org/.
- Liverpool COVID-19 Interactions. Drug Interactions database for COVID-19 Therapeutics. Accessed March 16, 2020. https://www.covid19-druginteractions.org/.
- Zhonghua Jie He Hu Xi Za Zhi. Multicenter collaboration group of Department of Science and Technology of Guangdong Province and Health Commission of Guangdong Province for chloroquine in the treatment of novel coronavirus pneumonia. [Expert consensus on chloroquine phosphate for the treatment of novel coronavirus pneumonia]. 2020; 43:E019.
- Sheahan TP et al. Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. Nature Communications 11, 222 (2020). https://doi.org/10.1038/s41467-019-13940-6.
- Wang M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Research 2020;30:269-271.
- WHO Clinical Management of Severe Acute Respiratory Infection when Novel Coronavirus (2019 – nCoV) Infection is suspected. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html
- Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA*. Published February 24, 2020.Xueting Y, et al. In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Clin Infect Dis. 2020. Doi: 10/1093/cid/ciaa237.
- HFSA/ACC/AHA Statement Addresses Concerns Re: Using RAAS Antagonists in COVID-19. March 17, 2020. https://www.acc.org/latest-in-cardiology/articles/2020/03/17/08/59/hfsa-acc-aha-statement-addresses-concerns-re-using-raas-antagonists-in-covid-19. Accessed March 20, 2020.
- Fang Lei. Are Patients with Hypertension and Diabetes Mellitus at increased risk for COVID-19 infection? The Lancet Published: March 11,2020 DOI:https://doi.org/10.1016/S2213-2600(20)30116-8
- Young BE, Ong SWX, Kalimuddin S, et al. Epidemiologic Features and Clinical Course of Patients Infected with SARS-CoV-2 in Singapore. JAMA. Published online March16, 2020. doi:10.1001/jama.2020.3204 (https://jamanetwork.com/journals/jama/fullarticle/2762688).
- WHO Clinical Management of Severe Acute Respiratory Infection when Novel Coronavirus (2019 – nCoV) Infection is suspected. Interim Guidance March 13, 2020.
- Vastag B. Old drugs for a new bug: influenza, HIV drugs enlisted to fight SARS. JAMA 2003, 290(13):1695-1696.
- Chan KS, Lai ST, Chu CM, Tsui E, Tam CY, Wong MM, Tse MW, Que TL, Peris JS. Treatment of severe acute respiratory syndrome with lopinavir/ritonavir: a multicenter retrospective match cohort study. Hong Kong Med J. 2003;9(6):399-406.
- Gamino-Arroyo E, Guerrero ML, McCarthy S, et al. Efficacy and Safety of Nitazoxanide in Addition to Standard of Care for the Treatment of Severe Acute Respiratory Illness. Clin Infect Dis. 2019 Nov 13;69(11):1903-1911.
- Xu X et al. Effective Treatment of Severe COVID-19 Patients with Tocilizumab. [pre-print-not peer reviewed] http://chinaxiv.org/abs/202003.00026 . Accessed March 20, 2020.
- Gautret et al. (2020) Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. International Journal of Antimicrobial Agents – In Press 17 March 2020 – DOI : 10.1016/j.ijantimicag.2020.105949.
- Gautret P, Lagier JC, Parola P, et al. Clinical and microbiological effect of a combination of hydroxychloroquine and azithromycin in 80 COVID-19 patients with at least a six-day follow up: an observational study. Preprint. https://www.mediterranee-infection.com/wp-content/uploads/2020/03/COVID-IHU-2-1.pdf?fbclid=IwAR0-uBG8W7rsx0YxGUfILvwl-Hr5uKs0VGyQEFqkhSL0pk3IvyQ7BF_KAwE

- Fujii T, et al. Effect of vitamin C, hydrocortisone, and thiamine vs hydrocortisone alone on time alive and free of vasopressor support among patients with septic shock: VITAMINS randomized clinical trial. JAMA. 2020;323(5):423-431. doi:10.1001/jama.2019.22176.
- Cao B et al. A trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19. NEJM. 2020 DOI: 10.1056/NEJMoa2001282.
- Lee DW, et al. ASTCT consensus grading for cytokine release syndrome and neurologic toxicity associated with immune effector cells. Biol Blood Marrow Transplant 2019:25:625-638.
- Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020:[Epub ahead of print]. https://www.ncbi.nlm.nih.gov/pubmed/32171076
- Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 2020:[Epub ahead of print]. https://www.ncbi.nlm.nih.gov/pubmed/32192578
- Teachey DT, Lacey SF, Shaw PA, et al. Identification of predictive biomarkers for cytokine release syndrome after chimeric antigen receptor T-cell therapy for acute lymphoblastic leukemia. Cancer Discov. 2016;6(6):664-679. https://www.ncbi.nlm.nih.gov/pubmed/27076371
- Roden DM, Harrington RA, Poppas A, Russo AM, Considerations for Drug Interactions on QTc in Exploratory COVID-19 (Coronavirus Disease 2019) Treatment, Journal of the American College of Cardiology (2020), doi: https://doi.org/10.1016/j.jacc.2020.04.016.
- Devaux CA, Rolain JM, Colson P et al. New insights on the antiviral effects of chloroquine against coronavirus: what to expect for COVID-19?. Int J Antimicrob Agents. 2020; 105938. (PubMed 32171740) (DOI 10.1016/j. ijantimicag.2020.105938)
- Cortegiani A, Ingoglia G, Ippolito M et al. A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19. J Crit Care. 2020; (PubMed 32173110) (DOI 10.1016/ j.jcrc.2020.03.005)
- Gao J, Tian Z, Yang X. Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. Biosci Trends. 2020; 14:72-73. (PubMed 32074550) (DOI 10.5582/bst.2020.01047)
- Yao X, Ye F, Zhang M et al. In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Clin Infect Dis. 2020; In Press. (PubMed 32150618) (DOI 10.1093/cid/ciaa237)
- Liu J, Cao R, Xu M et al. Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro. Cell Discov. 2020; 6:1-4. (PubMed 32194981) (DOI 10.1038/s41421-020- 0156-0)
- Sahraei Z, Shabani M, Shokouhi S et al. Aminoquinolines against coronavirus disease 2019 (COVID-19): chloroquine or hydroxychloroquine. Int J Antimicrob Agents. 2020; :105945. (PubMed 32194152) (DOI 10.1016/j.ijantimicag.2020.105945)
- Zhou D, Dai SM, Tong Q. COVID-19: a recommendation to examine the effect of hydroxychloroquine in preventing infection and progression. J Antimicrob Chemother. 2020; In Press. (PubMed 32196083) (DOI 10.1093/jac/ dkaa114)
- Chen J, Liu D, Li L et al. A pilot study of hydroxychloroquine in treatment of patients with common coronavirus disease-19 (COVID-19). J Zhejiang Univ. 2020; Mar. (DOI 10.3785/j.issn. 1008-9292.2020.03.03)
- US Food and Drug Administration. Letter of authorization: Emergency use authorization for use of chloroquine phosphate or hydroxychloroquine sulfate supplied from the strategic national stockpile for treatment of 2019 Coronavirus disease. 2020 Mar 28. From FDA website. (https://www.fda.gov/media/136534/download)
- US Food and Drug Administration. Fact sheet for health care providers emergency use authorization (EUA) of chloroquine phosphate supplied from the strategic national stockpile for treatment of COVID-19 in certain hospitalized patients. Dated 2020 Mar 28. From FDA website. (https://www.fda.gov/media/136535/download)
- US Food and Drug Administration. Fact sheet for health care providers emergency use authorization (EUA) of hydroxychloroquine sulfate supplied from the strategic national stockpile for treatment of COVID-19 in certain hospitalized patients. Dated 2020 Mar 28. From FDA website. (https://www.fda.gov/media/136537/download)
- Song Y, Zhang M, Yin L, et al. COVID-19 treatment: Close to a cure? – a rapid review of pharmacotherapies for the novel coronavirus. 2020. 2020030378. Doi: 10.20944/ preprints202003.0378.v1.
- Chen Z, Hu J, Zhang Z, et al. Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial. Preprint. https://www.medrxiv.org/ content/10.1101/2020.03.22.20040758v2.full.pdf.
- Molina JM, Delaugerre C, Goff JL, et al. No evidence of rapid antiviral clearance or clinical benefit with the combination of hydroxychloroquine and azithromycin in patients with severe COVID- 19 infection. Médecine et Maladies Infectieuses. 2020. Preprint. https://doi.org/doi:10.1016/j.medmal.2020.03.006.
- Mahevas M, Viet-Thi T, Roumier M, et al. No evidence of clinical efficacy of hydroxychloroquine in patients hospitalized for COVID-19 infection and requiring oxygen: results of a study using routinely collected data to emulate a target trial.
- Lakkireddy DR, Chung MK, Gopinathannair R, et al. Guidance for cardiac electrophysiology during the coronavirus (COVID-19) pandemic from the Heart Rhythm Society COVID-19 Task Force; Electrophysiology Section of the American College of Cardiology; and the Electrocardiography and Arrhythmias Committee of the Council on Clinical Cardiology, American Heart Association. 10.1161/CIRCULATIONAHA.120.047063.
- Sanders JM Monogue, ML, et al. Pharmacologic treatments for coronavirus disease 2019 (COVID-19): a review. JAMA. doi:10.1001/jama.2020.6019, published online April 13, 2020.
- Borba MG, Val, FF, Sampaio VS, et al. chloroquine diphosphate in two different dosages as adjunctive therapy of hospitalized patients with severe respiratory syndrome in the context of coronavirus (SARS-Co-V-2) infection: Preliminary safety results of a randomized, double-blinded, phase IIb clinical trial (CloroCovid-19 Study). medRxiv preprint doi: https://doi.org/10.1101/2020.04.07.20056424
- TOCIVID-19 trial: U.S. National Library of Medicine. ClinicalTrials.gov. Available from https://clinicaltrials.gov/ct2/show/study/NCT04317092 NLM identifier: NCT04317092
- COVACTA trial, US manufacturer trial: U.S. National Library of Medicine. ClinicalTrials.gov. Available from https://clinicaltrials.gov/ct2/show/study/NCT04320615 NLM identifier:

NCT04320615
- COVIDOSE trial: https://clinicaltrials.gov/ct2/show/NCT04331795 NCT04331795
- Massachusetts General Hospital trial: US manufacturer trial: U.S. National Library of Medicine. ClinicalTrials.gov. Available from https://clinicaltrials.gov/ct2/show/NCT04356937 NCT04356937
- Emory University Hospital / Winship Cancer Institute trial: US manufacturer trial: U.S. National Library of Medicine. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04361552 NCT04361552
- Chinese Clinical Trial Registry link: http://www.chictr.org.cn/
- Beigel JH, Tomasheck KM, et al. Remdesivir for the treatment of Covid-19 – preliminary report. New Engl J Med 2020. Downloaded from nejm.org on May 26, 2020.
- Bae YS, Van Voorhees AS, Hsu S, et al, "Review of Treatment Options For Psoriasis in Pregnant or Lactating Women: From the Medical Board of the National Psoriasis Foundation," J Am Acad Dermatol, 2012, 67(3):459-77.
- Angus DC and the members of the REMAP-CAP Investigators. Rffect of hydrocortisone on mortality and organ support in patients with severe covid-19: The REMAP-CAP COVID-19 corticosteroid domain randomized clinical trial. JAMA. doi:10.1001/jama.2020.17022 Published online September 2, 2020
- The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT)Working Group. Association between administration of systemic corticosteroids and mortality among critically ill patients with covid-19 a meta-analysis JAMA. doi:10.1001/jama.2020.17023 Published online September 2, 2020..