COVID-19 Therapies

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Currently, supportive care and acute measures should be applied to patients hospitalized with COVID-19 and associated complications. These may include the following:[1,2,30]

- Oxygen therapy for patients who develop respiratory distress, hypoxemia, or shock
- Empiric antimicrobials in the case of sepsis or secondary pneumonia
- Ventilatory support, and conservative fluid management in the case of acute respiratory distress syndrome
- Fluid boluses and vasopressors with septic shock
- The IDSA guideline panel suggests glucocorticoids for hospitalized patients with severe COVID-19 illness (with SpO2 ≤94% on room air, and those who require supplemental oxygen, mechanical ventilation, or ECMO). The guideline panel suggests against glucocorticoids for patients with COVID-19 without hypoxemia requiring supplemental oxygen.

Investigational therapies and vaccines

Several clinical trials are currently being performed to further the development and research of antiviral drugs against SARS-CoV-2 virus. At the present, there is no available data to support the recommendation of any of the following investigational therapies and vaccines for patients with confirmed/suspected COVID-19 infection:

Drug	**Mechanism of Action**	**Clinical Trials**
Antiviral Agents		
Favipiravir[24,25]	Nucleoside analogue that inhibits viral RNA polymerase enzyme and prevents replication of the viral genome.	China https://www.clinicaltrials.gov/ct2/show/NCT04310228?cond=COVID19 Italy https://clinicaltrials.gov/ct2/show/NCT04336904?cond=covid19

Remdesivir[3]	▪Incorporates into nascent viral RNA chains and produces premature termination of viral RNA transcription. ▪Has *in vitro* activity against SARS-CoV, MERS-CoV and some RNA viruses.	China https://clinicaltrials.gov/ct2/show/NCT04252664?term=remdesivir&cond=covid19&draw=2&rank=3 https://clinicaltrials.gov/ct2/show/NCT04257656?term=remdesivir&cond=covid19&draw=2 https://clinicaltrials.gov/ct2/show/NCT04252664?term=remdesivir&cond=covid19&draw=2 France https://clinicaltrials.gov/ct2/show/NCT04315948?cond=covid19 Norway https://clinicaltrials.gov/ct2/show/NCT04321616?cond=covid19 USA https://clinicaltrials.gov/ct2/show/NCT04302766?term=remdesivir&cond=covid19&draw=2 https://clinicaltrials.gov/ct2/show/NCT04323761?cond=covid19 https://clinicaltrials.gov/ct2/show/NCT04330690?cond=COVID-19 International multi-center sites https://clinicaltrials.gov/ct2/show/NCT04292730 https://clinicaltrials.gov/ct2/show/NCT04292899 https://clinicaltrials.gov/ct2/show/NCT04280705
Antimalarial		
Hydroxychloroquine[4-7]	From *in vitro* studies against SARS-CoV-2: ▪Changes the pH at the surface of the cell membrane and inhibits the fusion of the virus to the cell membrane. ▪Exerts antiviral effects by inhibiting nucleic acid	USA https://clinicaltrials.gov/ct2/show/NCT04308668 https://clinicaltrials.gov/ct2/show/NCT04328467?cond=COVID-19 https://clinicaltrials.gov/ct2/show/NCT04318444?cond=covid19 https://clinicaltrials.gov/ct2/show/NCT04328961?cond=COVID-19 https://clinicaltrials.gov/ct2/show/NCT04334148?cond=covid19 https://clinicaltrials.gov/ct2/show/NCT04335084?cond=covid19

	replication, glycosylation of viral proteins, virus assembly, new virus particle transport and release.	South Korea https://clinicaltrials.gov/ct2/show/NCT04330144?cond=COVID-19 Turkey https://clinicaltrials.gov/ct2/show/NCT04326725?cond=COVID-19 Spain https://clinicaltrials.gov/ct2/show/NCT04334928?cond=covid19 Mexico https://clinicaltrials.gov/ct2/show/NCT04318015?term=hydroxychloroquine&cond=covid19&draw=2
Hydroxychloroquine & azithromycin[8,9]	▪Hydroxychloroquine blocks viral entry by inhibiting virus/cell fusion from *in vitro* studies. ▪Azithromycin is a macrolide antibiotic that binds to the 50S ribosomal subunit of susceptible bacteria and interferes with microbial protein synthesis.	USA https://clinicaltrials.gov/ct2/show/NCT04336332?cond=covid19 https://clinicaltrials.gov/ct2/show/NCT04334382?cond=covid19#wrapper https://clinicaltrials.gov/ct2/show/NCT04335552?cond=covid19 Brazil https://clinicaltrials.gov/ct2/show/NCT04321278?cond=covid19 https://clinicaltrials.gov/ct2/show/NCT04329572?cond=COVID-19 Israel https://clinicaltrials.gov/ct2/show/NCT04322123?cond=covid19 Pakistan https://clinicaltrials.gov/ct2/show/NCT04328272?cond=COVID-19
Angiotensin II Receptor Blocker (ARB)		
Losartan[10-15]	Blocks the binding of angiotensin II to the AT1 receptor subtype in many tissues.	USA https://www.clinicaltrials.gov/ct2/show/NCT04311177?cond=COVID19 https://clinicaltrials.gov/ct2/show/NCT04312009?term=losartan&cond=covid19&draw=2
Immunomodulating Agents		

Bevacizumab[35]	A humanized monoclonal antibody that inhibits vascular endothelial growth factor (VEGF), a potent vascular permeability inducer. VEGF is associated with increased vascular permeability and pulmonary edema in acute lung injury and acute respiratory distress syndrome.	China and Italy https://www.clinicaltrials.gov/ct2/show/NCT04275414?term=bevacizumab&cond=COVID19&draw=2 https://www.clinicaltrials.gov/ct2/show/NCT04305106?term=bevacizumab&cond=COVID19&draw=2
Eculizumab[26]	A human monoclonal antibody that binds to complement proteins of the innate immune system, thus inhibiting formation of the membrane attack complex	USA https://www.clinicaltrials.gov/ct2/show/NCT04288713?cond=NCT04288713&draw=2&rank=1
Methylprednisolone and dexamethasone	Exert anti-inflammatory activity	China https://clinicaltrials.gov/ct2/show/NCT04273321?cond=COVID-19 Italy https://clinicaltrials.gov/ct2/show/NCT04323592?cond=covid19 South America https://clinicaltrials.gov/ct2/show/NCT04327401?cond=COVID-19 Spain https://clinicaltrials.gov/ct2/show/NCT04325061?cond=covid19
Sarilumab[16]	A human monoclonal antibody that inhibits interleukin-6 (IL-6) pathway by binding and blocking the IL-6 receptor.	USA http://www.news.sanofi.us/2020-03-16-Sanofi-and-Regeneron-begin-global-Kevzara-R-sarilumab-clinical-trial-program-in-patients-with-severe-COVID-19

		Italy https://clinicaltrials.gov/ct2/show/NCT04322188?cond=covid19
Siltuximab[27]	A human monoclonal antibody that inhibits interleukin-6 (IL-6) pathway by binding and blocking the IL-6 receptor.	Spain https://clinicaltrials.gov/ct2/show/NCT04329650?cond=COVID-19
Tocilizumab[17]	A human monoclonal antibody that inhibits interleukin-6 (IL-6) pathway by binding and blocking the IL-6 receptor.	USA https://clinicaltrials.gov/ct2/show/NCT04331795?cond=covid19 China http://www.chictr.org.cn/showprojen.aspx?proj=49409 Denmark https://clinicaltrials.gov/ct2/show/NCT04322773?cond=covid19 Italy https://clinicaltrials.gov/ct2/show/NCT04317092?cond=covid19 https://clinicaltrials.gov/ct2/show/NCT04332913?cond=covid19 Switzerland https://clinicaltrials.gov/ct2/show/NCT04335071?cond=covid19 International multi-center sites https://clinicaltrials.gov/ct2/show/NCT04320615?cond=covid19
JAK (Janus kinase) Inhibitors		
Baracitinib[36]	Inhibits viral endocytosis by numb-associated kinases (NAK) → prevent cytokine storm and block early stages of viral entry and spread into host cells.	Canada https://clinicaltrials.gov/ct2/show/NCT04321993?cond=covid19 Italy https://www.clinicaltrials.gov/ct2/show/NCT04320277

Ruxolitinib[36]	Inhibits viral endocytosis by numb-associated kinases (NAK) → prevent cytokine storm and block early stages of viral entry and spread into host cells.	Mexico https://clinicaltrials.gov/ct2/show/NCT04334044?cond=covid19 USA https://clinicaltrials.gov/ct2/show/NCT04337359?cond=covid19
Miscellaneous		
Bromhexine HCl[31]	A mucolytic drug that increases the production of serous mucus in the respiratory tract, thereby making the phlegm thinner and less viscous. The drug exerts a secretomotoric effect, allowing the cilia to transport the phlegm out of the lungs.	China https://www.clinicaltrials.gov/ct2/show/NCT04273763?cond=Bromhexine+HCl&draw=2
Camostat Mesilate[32]	Inhibits TMPRSS2, a serine protease that primes the spike protein of highly pathogenic human coronavirus (i.e., MERS-CoV and SARS-CoV) and facilitates its entry into the host cell, and blocks the spread and pathogenesis of SARS-CoV in a mouse model study.	Denmark https://clinicaltrials.gov/ct2/show/NCT04321096?cond=covid19 Germany https://clinicaltrials.gov/ct2/show/NCT04338906?cond=covid19
Convalescent plasma[18]	Infusing patients with antibody-rich plasma from people who have recovered from COVID-19 infection to	Colombia https://clinicaltrials.gov/ct2/show/NCT04332835?cond=covid19 Iran https://clinicaltrials.gov/ct2/show/NCT04327349?cond=COVID-19

	boost their passive immunity against SARS-CoV-2.	USA https://clinicaltrials.gov/ct2/show/NCT04325672?cond=covid19
Dapagliflozin[28,29]	▪Inhibits sodium-glucose cotransporter 2 (SGLT2), thereby reducing reabsorption of filtered glucose, lowering the renal threshold for glucose, and increasing urinary glucose excretion. ▪SGLT2 have demonstrated to have potent heart and renal-protective effects in patients with type 2 diabetes, heart failure and/or chronic kidney disease and may protect the vital organ systems in the setting of COVID-19 May improve diabetic control as well which may also improve response	USA https://clinicaltrials.gov/ct2/show/NCT04350593
Tradipitant[33,34]	Inhibits the substance P neurokinin-1 receptor, which is involved in the neuroinflammatory processes that lead to significant lung injury following viral infections.	USA https://clinicaltrials.gov/ct2/show/NCT04326426?term=tradipitant&draw=2&rank=2
Vitamin D[19-23]	▪A hormone precursor produced by our own body with the help of sunlight.	Spain https://clinicaltrials.gov/ct2/show/NCT04334005?cond=covid19

	▪Has an important role on adaptive immunity and cellular differentiation, maturation and proliferation of several immune cells.	
Vaccines		
COVID-19/aAPC	▪Applies lentivirus modification of immune modulatory genes and viral minigenes to artificial antigen presenting cells (aAPCs). ▪COVID-19/aAPCs are inactivated for proliferation and tested for safety in human subjects.	China https://clinicaltrials.gov/ct2/show/NCT04299724?recrs=abdfm&cond=covid19&draw=2
mRNA-1273	▪Encodes a prefusion-stabilized form of the S (Spike) protein, which is part of the viral envelope. ▪Results in transcription of certain coronavirus-S-like proteins, which are the proteins that the virus uses to gain entry into the lung epithelial cells. ▪Antibodies are then formed by those vaccinated against the S protein.	USA https://clinicaltrials.gov/ct2/show/NCT04283461?term=mRNA-1273&cond=COVID-19&cntry=US&state=US%3AWA&draw=2&rank=1
Bacille Calmette-Guérin (BCG)	BCG is a vaccine against tuberculosis, with protective non-specific effects against other respiratory tract	Australia https://clinicaltrials.gov/ct2/show/NCT04327206?cond=COVID-19 Netherlands

	infections in *in vitro* and *in vivo* studies.	https://clinicaltrials.gov/ct2/show/NCT04328441?cond=COVID-19

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