COVID-19 Therapies

Currently, supportive care and acute measures should be applied to patients hospitalized with COVID-19 and associated complications. These may include the following:\textsuperscript{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 $\leq 94\%$ 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:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of Action</th>
<th>Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>\textit{Antiviral Agents}</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Remdesivir<sup>3</sup> | • 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  
France  
Norway  
USA  
International multi-center sites  
https://clinicaltrials.gov/ct2/show/NCT04292730  
https://clinicaltrials.gov/ct2/show/NCT04292899  
https://clinicaltrials.gov/ct2/show/NCT04280705 |
| Antimalarial | 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  

Hydroxychloroquine<sup>4-7</sup>: 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
| Hydroxychloroquine & azithromycin\(^8,9\) | South Korea  
Turkey  
Spain  
Mexico  
|---|---|
| ▪ 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/NCT04334382?cond=covid19#wrapper  
Brazil  
Israel  
https://clinicaltrials.gov/ct2/show/NCT04322123?cond=covid19  
Pakistan  
| **Angiotensin II Receptor Blocker (ARB)** |  
**Losartan**\(^10-15\)  
Blocks the binding of angiotensin II to the AT1 receptor subtype in many tissues. |  
USA  
<p>| <strong>Immunomodulating Agents</strong> |  |</p>
<table>
<thead>
<tr>
<th>Drug</th>
<th>Description</th>
<th>Locations</th>
</tr>
</thead>
</table>
| Bevacizumab   | 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  
| Eculizumab    | 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  
Italy  
South America  
Spain  
| Sarilumab     | A human monoclonal antibody that inhibits interleukin-6 (IL-6) pathway by binding and blocking the IL-6 receptor. | USA  
<table>
<thead>
<tr>
<th>Country</th>
<th>Clinical Trial Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Italy</td>
<td><img src="https://clinicaltrials.gov/ct2/show/NCT04332913?cond=covid19" alt="Clinical Trial Link" /></td>
</tr>
<tr>
<td>Spain</td>
<td><img src="https://clinicaltrials.gov/ct2/show/NCT04320277" alt="Clinical Trial Link" /></td>
</tr>
<tr>
<td>USA</td>
<td><img src="https://clinicaltrials.gov/ct2/show/NCT04331795?cond=covid19" alt="Clinical Trial Link" /></td>
</tr>
<tr>
<td>China</td>
<td><img src="http://www.chictr.org.cn/showprojen.aspx?proj=49409" alt="Clinical Trial Link" /></td>
</tr>
<tr>
<td>Denmark</td>
<td><img src="https://clinicaltrials.gov/ct2/show/NCT04322773?cond=covid19" alt="Clinical Trial Link" /></td>
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<tr>
<td>Switzerland</td>
<td><img src="https://clinicaltrials.gov/ct2/show/NCT04335071?cond=covid19" alt="Clinical Trial Link" /></td>
</tr>
<tr>
<td>International multi-center sites</td>
<td><img src="https://clinicaltrials.gov/ct2/show/NCT04320615?cond=covid19" alt="Clinical Trial Link" /></td>
</tr>
</tbody>
</table>

**Siltuximab**

A human monoclonal antibody that inhibits interleukin-6 (IL-6) pathway by binding and blocking the IL-6 receptor.

**Tocilizumab**

A human monoclonal antibody that inhibits interleukin-6 (IL-6) pathway by binding and blocking the IL-6 receptor.

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**JAK (Janus kinase) Inhibitors**

**Baracitinib**

Inhibits viral endocytosis by numb-associated kinases (NAK) → prevent cytokine storm and block early stages of viral entry and spread into host cells.

**Canada**

![Clinical Trial Link](https://clinicaltrials.gov/ct2/show/NCT04321993?cond=covid19)

**Italy**

![Clinical Trial Link](https://www.clinicaltrials.gov/ct2/show/NCT04320277)
| **Ruxolitinib**<sup>36</sup> | Inhibits viral endocytosis by numb-associated kinases (NAK) to prevent cytokine storm and block early stages of viral entry and spread into host cells. | Mexico  
USA  
<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Miscellaneous</strong></td>
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</tbody>
</table>
| **Bromhexine HCl**<sup>31</sup> | 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  
| **Camostat Mesilate**<sup>32</sup> | 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  
Germany  
| **Convalescent plasma**<sup>18</sup> | Infusing patients with antibody-rich plasma from people who have recovered from COVID-19 infection to  | Colombia  
Iran  
<table>
<thead>
<tr>
<th>Drug</th>
<th>Description</th>
<th>Reference</th>
<th>Country</th>
<th>Clinical Trial Link</th>
</tr>
</thead>
</table>
| **Dapagliflozin**<sup>38,29</sup> | • 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/NCT04325672?cond=covid19> |
| **Tradipitant**<sup>33,34</sup> | 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**<sup>19-23</sup> | • 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**

<table>
<thead>
<tr>
<th>Vaccine Type</th>
<th>Description</th>
<th>Country</th>
<th>Link</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRNA-1273</td>
<td>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.</td>
<td>USA</td>
<td><a href="https://clinicaltrials.gov/ct2/show/NCT04283461?term=mRNA-1273&amp;cond=COVID-19&amp;entry=US&amp;state=US%3AWA&amp;draw=2&amp;rank=1">https://clinicaltrials.gov/ct2/show/NCT04283461?term=mRNA-1273&amp;cond=COVID-19&amp;entry=US&amp;state=US%3AWA&amp;draw=2&amp;rank=1</a></td>
</tr>
</tbody>
</table>

Netherlands
infections in *in vitro* and *in vivo* studies.


References

1. www.who.int/health-topics/coronavirus
9. French study on combination HCQ and azithromycin
17. **Effective Treatment of Severe COVID-19 Patients with Tocilizumab**
18. **Recommendations for Investigational COVID-19 Convalescent Plasma**