There are many therapeutics under early investigation for treatment of COVID-19 for which there is currently insufficient clinical data to recommend either for or against. This overview is not a comprehensive summary, but a list of therapeutics with strong biological plausibility that are available in the United States and are or will be studied by clinical trial.

<table>
<thead>
<tr>
<th>Class/Drug</th>
<th>Mechanism of Action</th>
<th>Notable Publications*</th>
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</thead>
</table>
| Anakinra                  | • Interleukin (IL)-1 receptor antagonist; blocks activity of the proinflammatory cytokines IL-1α and IL-1β.                                                                                                          | Cavalli, June 2020  
Huet, May 2020                                                                        |
| Baricitinib               | • Janus kinase (JAK) 1 and 2 inhibitor; inhibits JAK1-2 mediated cytokine release.  
• Disrupts endocytosis regulators and cyclin G-associated kinase; may reduce inflammation and interfere with intracellular virus assembly.                     | Cantini, April 2020                                                               |
| Colchicine                | • Exhibits broad anti-inflammatory and immunomodulatory properties.  
• Disrupts microtubule formation and reduces chemotaxis, phagocytosis and migration of neutrophils.                                                                                                             | Tardif, January 2021  
Della-Torre, August 2020  
Lopes, August 2020  
Gendelman, July 2020  
Deftereos, June 2020                                                             |
| Interferons               | • Modulate the immune response in specific—not all—viral infections.  
• Bind to interferon-α and -β receptors on the cell membrane, resulting in various transcription factor phosphorylation. Subsequent activation of interferon-stimulated genes leads to immunomodulatory effects and interference with viral replication. | Monk, November 2020  
Wang, July 2020  
Davoudi-Monfared, May 2020  
Zhou, May 2020  
Hung, May 2020                                                                       |
| Intravenous immunoglobulin| • Derived from pooled plasma; contains antibodies typically present in adult human blood.  
• May provide passive immune protection from viral infections via modulation of inflammation.                                                                                                           | Sakoulas, November 2020  
Gharebaghi, October 2020  
Xie, August 2020  
Sakoulas, July 2020  
Shao, April 2020                                                                    |
| Ruxolitinib               | • Janus kinase (JAK) 1 and 2 inhibitor; inhibits JAK1-2 mediated cytokine release.  
• Disrupts endocytosis regulators and cyclin G-associated kinase; may reduce inflammation and interfere with intracellular virus assembly.                      | Zhang, August 2020  
Kow, August 2020  
De Spiegeleer, July 2020                                                            |
| Statins                   | • Statins have anti-inflammatory and immunomodulatory properties that may allow for lung protection in the setting of infection.                                                                                   | Zhang, August 2020  
Kow, August 2020  
De Spiegeleer, July 2020                                                            |
| Calcifediol/Vitamin D     | • Prohormone of the active form of vitamin D3, calcitriol (1,25-dihydroxyvitamin D3).                                                                                                                             | Murai, February 2021  
Patchen, February 2021  
Castillo, October 2020                                                               |
• Binds to the vitamin D receptor in target tissues and activates vitamin D responsive pathways that result in increased intestinal absorption of calcium and phosphorus and reduced parathyroid hormone synthesis.

*Published clinical studies (including preprints). Excludes case reports and case series.