**Supplementary Table 3.** **Newer drugs being tried in the treatment of patients with COVID-19 and its possible effects on the liver**

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| --- | --- | --- |
| Drug | Class | Potential to cause DILI |
| Molnupiravir | **Antiviral**Introduces copying errors during viral RNA replication of the SARS-CoV-2 virus | Seems rareMore data needed |
| Nitazoxanide | **Antiviral**Thiazolide antiparasitic agent; inhibits replication of a broad range of respiratory viruses in cell cultures, including SARS-CoV-2 | Immunoallergic reactions leading to mild elevations of liver enzymes have been reported |
| Niclosamide | **Antiviral**Anthelmintic agent that has potential use as an antiviral agent | Extremely rare |
| Rintatolimod | **Antiviral**Toll-like receptor 3 agonist | Data needed to establish safety on liver |
| Bemcentinib | **Antiviral**Oral AXL kinase inhibitor | Data needed to establish safety on liver |
| Umifenovir | **Antiviral**Targets the spike glycoproteins of SARS-CoV-2 | Data needed to establish safety on liver |
| Plitidepsin | **Antiviral**Belongs to the class of didemnins; targets EF1A, which is key to multiplication and spread of the virus | Transient transaminase elevations were frequent but achieved grade 3 or 4 in only 10% of patientss1 |
| VIR-2703 | **Antiviral**Drug targets small interfering RNA which leads to gene silencing | Data needed to establish safety on liver |
| AT-527 | **Antiviral**Purine nucleotide prodrug that inhibits RNA polymerase enzyme | Data needed to establish safety on liver |
| Trabedersen | **Antiviral**Antisense oligonucleotide that inhibits transforming growth factor-beta 2 expression; inhibits Viral replication | Data needed to establish safety on liver |
| Apilimod | **Antiviral**Inhibits the lipid kinase enzyme PIKfyve; interferes with the entry and trafficking of the SARS-CoV-2 virus | Data needed to establish safety on liver |
| Bamlanivimab | **Antiviral**Neutralizing IgG1 monoclonal antibody directed against the spike protein of SARS-CoV-2; blocks viral attachment and entry | Data needed to establish safety on liver |
| Infliximab | **Immunomodulator**Inhibits tumor necrosis factor | 1) Can cause elevation of aminotransferases and ALP; usually not severe and resolves in 4 to 12 weeks of stopping therapys22) Hepatocellular injury typically associated with autoimmune markerss23) Cholestatic injury, can arise as early as a few days to up to 24 weeks after starting therapys34) Liver injury due to reactivation of chronic hepatitis Bs4 |
| Abatacept | **Immunomodulator**Prevents full activation of T cells | Aminotransferase elevations occur in 2% to 3% of treated patients, causing liver injury by triggering autoimmunity has been reported;s5 liver injury due to reactivation of chronic hepatitis Bs6 |
| Cenicriviroc | **Immunomodulator**Blocks 2 chemokine receptors, CCR2 and CCR5 | Safety established from fatty liver studies; data needed to establish safety on liver in patients with COVID-19 |
| Bevacizumab  | **Immunomodulator**Anti-vascular endothelial growth factor; acts to decrease vascular permeability and pulmonary edema in patients with SARS-CoV2 | Reported to be safe but as the drug inhibits angiogenesis, it can potentially affect liver regeneration |
| Tradipitant | **Immunomodulator**NK-1 receptor antagonist | Data needed to establish safety on liver |
| Sargramostim | **Immunomodulator**Inhaled colony-stimulating factor; reduce the risk of secondary infection; stimulate alveolar epithelial cell healing during lung injury | Safe; occasional rise of ALP, but postulated to be from the bone instead of the liver |
| Remestemcel-L | **Immunomodulator**Allogeneic mesenchymal stem cell; plays a role in downregulation of proinflammatory cytokines | Data needed to establish safety on liver |
| Ibudilast | **Immunomodulator**Phosphodiesterases 4 and 10 inhibitor and a macrophage migration inhibitory factor inhibitor that suppresses proinflammatory cytokines | More data needed; occasional reports of GGT elevation noted with its uses7 |

AXL, anexelekto; CCR, chemokine receptor; EF1A, eukaryotic elongation factor 1A; GGT, gamma glutamyl transpeptidase; IgG, immunoglobulin G; MIF, macrophage migration inhibitory factor.

**References**

s1. Izquierdo MA, Bowman A, García M, Jodrell D, Martinez M, Pardo B, *et al*. Phase I clinical and pharmacokinetic study of plitidepsin as a 1-hour weekly intravenous infusion in patients with advanced solid tumors. Clin Cancer Res 2008;14(10):3105-3012. doi: 10.1158/1078-0432.CCR-07-1652.

s2. French JB, Bonacini M, Ghabril M, Foureau D, Bonkovsky HL. Hepatotoxicity associated with the use of anti-TNF-α agents. Drug Saf 2016;39(3):199-208. doi: 10.1007/s40264-015-0366-9.

s3. Wong F, Al Ibrahim B, Walsh J, Qumosani K. Infliximab-induced autoimmune hepatitis requiring liver transplantation. Clin Case Rep 2019;7(11):2135-2139. doi: 10.1002/ccr3.2456.

s4. Miyake Y, Hasebe A, Tanihira T, Shiraishi A, Imai Y, Tatsukawa H, *et al*. Hepatitis B virus reactivation induced by infliximab administration in a patient with Crohn's disease. Case Reports Hepatol 2013;2013:461879. doi: 10.1155/2013/461879.

s5. Iwanaga N, Origuchi T, Terada K, Ueki Y, Kamo Y, Kinoshita N, *et al*. Rheumatoid arthritis complicated with severe liver injury during treatment with abatacept. Mod Rheumatol 2014;24(5):874-876. doi: 10.3109/14397595.2013.844399.

s6. Talotta R, Atzeni F, Sarzi Puttini P. Reactivation of occult hepatitis B virus infection under treatment with abatacept: a case report. BMC Pharmacol Toxicol 2016;17:17. doi: 10.1186/s40360-016-0060-2.

s7. Rolan P, Gibbons JA, He L, Chang E, Jones D, Gross MI, *et al*. Ibudilast in healthy volunteers: safety, tolerability and pharmacokinetics with single and multiple doses. Br J Clin Pharmacol 2008;66(6):792-801. doi: 10.1111/j.1365-2125.2008.03270.x.