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# A Conspectus Study in Treatment of COVID-19 using Monoclonal Antibodies

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**Abstract:** ***To prevent and/or neutralise the coronavirus in infected patients, researchers are rushing to create medicines based on antibodies. The promise for understanding disease pathophysiology was initially provided by the virus's genetic and structural resemblance to the coronavirus associated with severe acute respiratory syndrome (SARS-CoV). Reports of individual monoclonal antibodies against COVID-19 have been published by researchers. The main type of biotherapeutics used in passive immunotherapy to combat viral infection is monoclonal antibodies. In the treatment of numerous diseases, the therapeutic potential of monoclonal antibodies has long been acknowledged. Neutralising monoclonal antibodies prevent the interaction between the viral spike and the ACE 2 receptor, which is present on a variety of cell types, from causing viral infection. The creation of novel monoclonal antibodies treatments for oncology, inflammation, and rare diseases as well as infectious diseases will likely be significantly impacted using the manufacturing, control, and chemistry methodologies because they create a new standard for rapidity, safety, and clinical advantage. Additional investigation into the pathogenesis of COVID-19 may help to pinpoint the best treatment targets for the creation of targeted antivirals to combat this recently discovered disease. This brief review addressed a number of MABs, including an overview of the SARS-CoV-2 immunological response, details on the structure is the spike protein of the SARS-CoV-2 virus, a primary target of the MABs, details on the MABs' mechanisms of action, comparisons to successful vaccines, and an update on the COVID-19 clinical trials using MABs.***

**Keywords:** Monoclonal antibodies, SARS-COV, SARS-COV-2, COVID-19 biotherapy

## 1. Introduction

A normal immune system reaction to an infection is the production of an antibody, which is a protein. A molecule called a monoclonal antibody created in lab mimics or strengthens the immune system's defences against an enemy like cancer or an infection. A virulent coronavirus illness (COVID-19) was first identified in Wuhan, China, is also known to be called as Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) around the end of the year 2019. [1] Very quickly, it began to spread to neighbouring nations and quickly grew to epidemic proportions. Coronaviruses (CoVs), which range in complexity from a typical cold virus to more complicated conditions like Middle East respiratory sickness (MERS) & SARS-CoV, are found among the avian and mammalian species. [2, 3] However, the precise origin of animal reservoirs, enzymatic transmission pathways, and SARS-CoV-2 are still unknown. It is thought that they are bat-borne. Coronaviruses are enclosed viruses, pleomorphic or spherical encapsulated particles comprising positive-sense single-stranded RNA coupled using a nucleoprotein in the capsid and composed of the spike (s) proteins. [4] In terms of morphology as well as chemical structure, coronaviruses are identical to one another. There is at present no known vaccination or therapy for COVID-19, despite several attempts to provide effective COVID-19 treatment options. [5] S proteins, which are crucial for virus entrance and the cycle of viral duplicated within the host cell, have been the prime topic of extensive research on anti-viral compounds. [6] A possibility for studying the pathophysiology of this illness was generated by the structural and genetic resemblances between the SARS-CoV and a virus. The COVID-19 biotherapy might be of interest because monoclonal antibodies (MABs) have been shown to be more effective against other coronaviruses. [7] Effective treatments for SARS-CoV-2 may include particular therapeutic agents, and broad-spectrum antiviral drugs (BSA) that immediately interrupts each stage of the viral lifecycle, or protein receptors situated at the cellular membrane of the host. They consist of the fusion inhibitor peptide, anti-SARS-Coronavirus-2 neutralising antibodies, monoclonal antibodies against ACE2 and protease inhibitor. [8] Monoclonal antibodies (MAB) continue to be an potent treatment option for the management plan of COVID-19 illness and associated consequences, particularly in the elderly. [9]More than 50 clinical studies with monoclonal antibodies are being carried out in various nations throughout the world, with just a handful of them approaching the end of the third and fourth phases. [10]It is crucial that MABs, which are currently used to treat illnesses like as the respiratory syncytial virus and Ebola (RSV), are debated in the scientific fields in light of the FDA's recent emergency use authorisation (EUA) for casirivimab and imdevimab. [11]This succinct review covered a variety of MABs, including an overview regarding SARS-CoV-2 immunological response, data on the SARS-CoV-2 spike protein's composition, which is a main objective of the MABs, information on the MABs' mechanisms of action, comparisons to effective vaccines, and an update on the clinical-observational trials using MABs for COVID-19. [12, 13] The development of therapeutic approaches to combat coronavirus infection has received significant attention. The identification of anti-viral compounds that target the spike protein, which promotes viral passage, and their ability to trigger host immune counters and generate infected individuals' defensive antibody responses have been the subject of much investigation. [14]In this study, we focus on the potential therapeutic use of neutralising antibodies that have demonstrated promising activity against SARS-CoV or MERS CoV and may be utilised suitably for SARS-CoV-2 prevention and medical treatment. [15]

**Therapeutic Intervention Concerning COVID-19:**

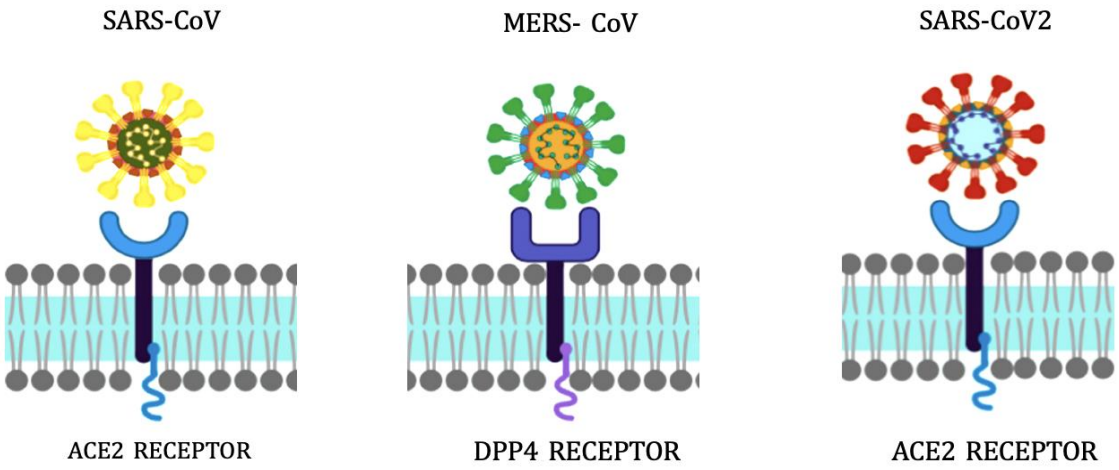


**Figure 1:** Binding domain of different COVID-19 viruses

The both SARS & MERS-COVs envelope spike proteins as displayed schematically, and they bind to the host Dipeptidyl peptidase 4 (DPP-4) enzyme as well as the receptors of angiotensin-converting 2 enzyme (ACE2). [16]Similar to SARS-CoV, every new coronavirus SARS-CoV 2 enters the host through using the ACE2 receptor. [17, 18] (Figure 1) Spike protein's receptor binding domain binds with the cellular receptor to induce membrane fusion and start the life cycle of the virus. (Figure ***2***) [19, 20]

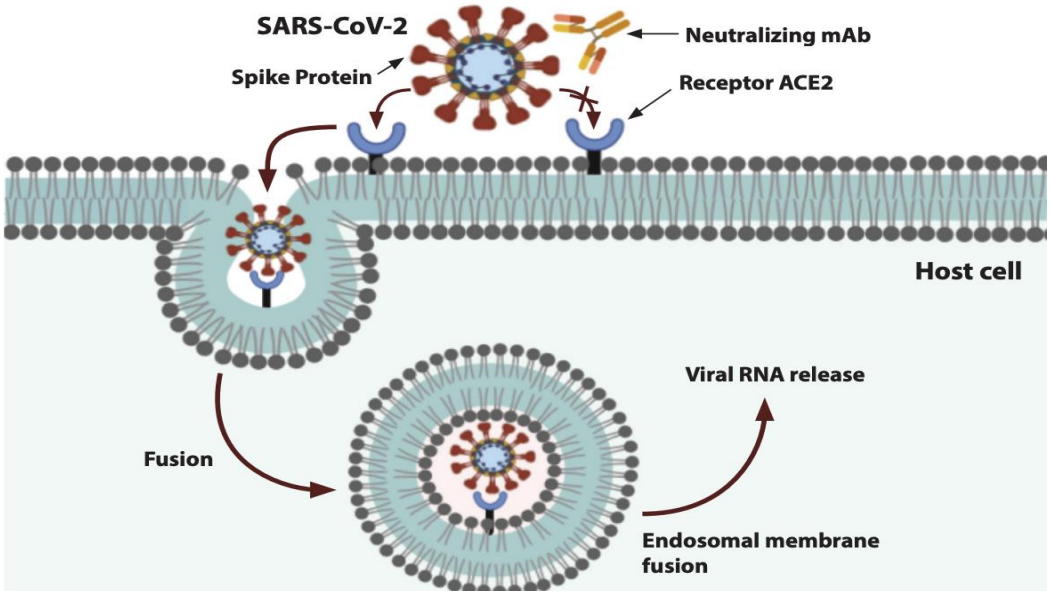


**Figure 2:** Life cycle of SARS-COV-2

Schematic representations of the host receptors DPP4 and ACE2 are two examples of angiotensin-converting enzymes for the SARS CoV as well as MERS-CoV microbes envelope spike proteins are presented. [21, 22] The SARS CoV 2, a pathogenic coronavirus passages the host through the ACE2 receptor, much like SARS-CoV did. [23, 24]Binding of an individual protein's receptor region surge interacts with the cellular binding domain to cause fusing of the membrane to begin the virus' life cycle. [25, 26]

**Specific monoclonal antibodies counter to SARS-COV-2:**

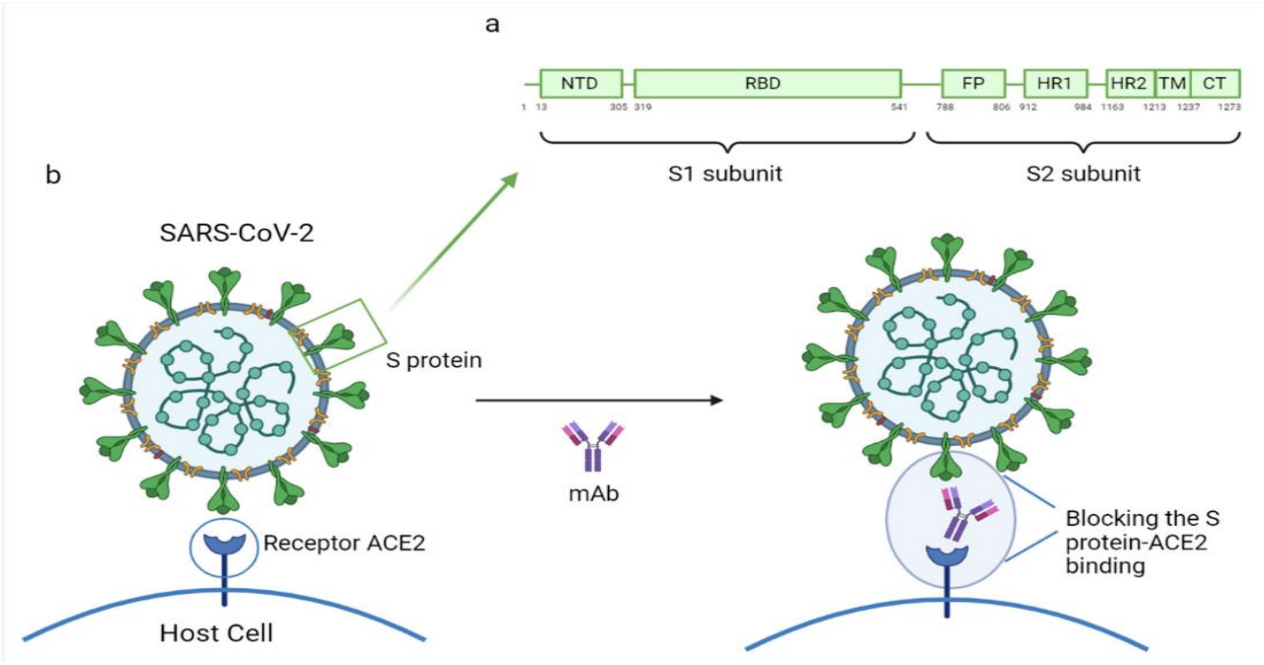


**Figure 3:** Binding of specific MAB to SARS-COV-2

Both SARS CoV as well as SARS CoV 2 quite identical with regards to structural makeup and genetic make-up, corresponding to phylogenetic study. This gave research persons an initiating point for their early inquiry and favored in their understanding of the aetiology of COVID-19. [27] In fact, both coronaviruses' glycosylated spike (S) proteins share 77.5% of their elementary amino acid sequences. [28] These coronaviruses bears S proteins on their surface, and they perform a pivotal role in infection. By attaching to the receptor-binding site for angiotensin II in the host cell, they facilitate the viral host cell passage (ACE2). (Figure 3) [29]Transmembrane (TM), the concise intracellular C-terminal section, and the extracellular N-terminus blend the 1273 amino acids (aa) that compose the SARS-CoV-2 S protein. N-terminus domain, which is where, a signal peptide of some aa is present (1–13 residues). S1 and S2 subunits comprise the last two substantial portions of the protein. [30] The N-terminal domain (NTD) as well as the binding domain for receptor make up the S1 component, which has a length of 14-685 amino acids (RBD). [31] The S2 component (686-1273 aa) is a part of the fusing membranes of the host and virus cells, as well as the subsequent genome of the virus is released and it penetrates into the host cell. [32] It contains the TM domain, cytoplasm domain, heptapeptide repeat sequence 1 (HR1), fusion peptide (FP), HR2, and HR2. Since it enables protein spikes to attach towards the cell receptor ACE2, considered to be an important target for neutralising antibodies (NABs), the RBD region. [33]

**Non-specific mabs targeting SARS-COV-2:**

The COVID-19 disease's severity may be influenced by the immune responses that the virus triggers, and this is the focus of the MABs which now utilised in medical facilities to treat COVID-19. One of these immunological reactions is regarded as a "cytokine storm, " one potentially fatal chronic inflammation disease, and it includes the abrupt release of massive quantities of certain cytokines into the bloodstream. [34]Biological drugs that are anti-IL-6/IL-6R has acts in the handling of COVID-19 since the inception of the illness since one among the main pro-inflammatory cytokines discovered among people with this condition is IL 6. The MABs that are utilised for the therapy of patients having COVID-19 are high levels of IL-6 are siltuximab, sarilumab, and tocilizumab. [35]There are patient based studies being done for assessing their effectiveness, that has not so far been completely established. [36]

Clinical studies are also being conducted with various non-SARS-CoV-2 specific MABs like pembrolizumab, itolizumab, mavrilimumab, gimsilumab, itolizumab, clazakizumab, eculizumab, mavrilimumab and emapalumab, whose treatment goals are unreachable IL-6/IL-6R Anakinra is an anti-IL-1R protein therapy that also been utilised. To yet, none of them have yielded definitive findings. Due to their extensive application, we will concentrate pointedly on anti-IL-6/IL-6R MABs in this study as well as how they are is employed to heal the cytokine storm related to COVID-19. [37, 38]

***1) TOCILIZUMAB (TCZ):***

A humanised IgG1 monoclonal antibody called TCZ prevents IL-6 membrane-bound and soluble receptors from releasing signals. Different autoimmune illnesses including systemic juvenile idiopathic arthritis and rheumatoid arthritis are routinely treated with it. [39]

Off-label utilisation of MABs in patients suffering from COVID-19 quickly became a norm in several regions of the world during the pandemic epidemic. Anti-IL-6 MABs were detected as effective for treating serious patients from the arsenal based on medications put out as anti-COVID-19 possibilities. [40]Given its bigger more supply and time spent on the market, and accessibility in with the help of an intravenous (IV) medication, TCZ has been the one of these that hospitals have used the most frequently. Several randomised clinical trials as well as a significant number of observational studies are starting to evaluate its safety and effectiveness in the management of COVID-19. [41]There have been 78 clinical studies registered as of this writing. [42, 43]

***2) SARILIMAB:***

Human IgG1 MAB sarilumab suppresses IL-6-mediated signaling by targeting IL-6 receptors that are membrane-bound and soluble (IL-6Rs). [44]It is advised in order to treat moderate-to-serious adult patient's rheumatoid arthritis (RA) when used in conjunction with methotrexate. [45, 46]

***3) SILTUXIMAB:***

A chimeric human-murine monoclonal antibody called siltuximab blocks from human IL-6 interacting with both membrane-bound and soluble IL-6 receptors (IL-6R). [47] It has endorsement in order to treat adult patients with Multicentric Castleman's disease (MCD)., [48]

***4) LENZILUMAB:***

A case-control study on patients receiving lenzilumab shown an 80% decrease in the invasive ventilation and/or mortality relative hazard in contrast to the control group. [49]The study used a humanised MAB against interleukin-23 (IL-23). Lenzilumab-treated individuals had a median reduction in ARDS resolution time of one day and early hospital release compared to control group patients who had a double-time before discharge and ARDS resolution time of eight days. [50]

## 2. Conclusion

Since the start of the pandemic, MABs have been seen altogether as viable alternative medicine for COVID-19, despite the fact that their production takes a long time and costs money, particularly to combat novel infections. [51] Numerous clinical studies for SARS-CoV-2 specific as well as non-specific MABs are presently underway. [52]While SARS-CoV-2 definite monoclonal antibodies have shown appreciable levels of effectiveness, the results of clinical research for MABs not specific to SARS-CoV-2 are justifying contentious because they have not yet been proven effective. The goal should be to create monoclonal antibodies that have a narrow target audience, can be produced for a small fraction of the existing cost, and are extremely effective. [6]

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