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# Monoclonal Antibodies vs. Symptomatic Treatment of Hospitalized Patients with COVID-19

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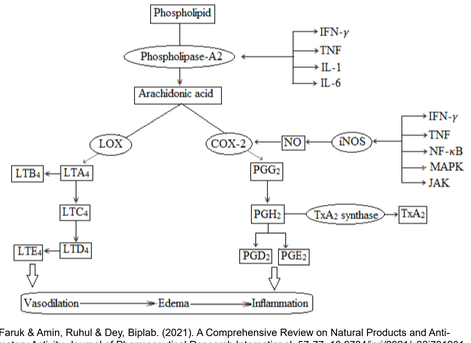
## Abstract

The SARS-CoV-2 virus, or COVID-19, was the virus responsible for the worldwide pandemic declared in March, 2020. Individuals can experience a wide variety of symptoms ranging from fever, fatigue, cough, and, in more severe cases, hypoxia requiring invasive mechanical ventilation (IMV). Until recently, symptomatic care was the protocol for patients infected with COVID-19. The use of oxygen for mild hypoxia and antipyretics for fevers was considered the standard of care (SOC). The use of antiviral medications, such as monoclonal antibodies, has been proposed in the treatment of acute COVID-19 infection. The purpose of this literature review is to determine if monoclonal antibodies could be considered as treatment options for high-risk patients hospitalized with COVID-19. A literature review was performed on PubMed using the following MESH terms: COVID-19, monoclonal antibodies, and hospitalization. Articles from 2020 to the present were included in the search. Studies were limited to randomized control trials and clinical trials. Out of 97 total search results, 20 articles were relevant to the search. 10 articles were removed due to the studies being performed as outpatient procedures. Two studies were removed as they were reviews. There are three common goals throughout the studies analyzed in this literature review regarding the use of monoclonal antibodies in patients with COVID-19. The first goal is to decrease the length of hospital admission, the second is to decrease the severity of symptoms, shown by a decrease in inflammatory markers, that may be lethal to more fragile patients, and the third is to reduce the overall mortality of COVID-19. The literature review showed monoclonal antibodies are beneficial when their mechanism of action causes direct inhibition of the inflammatory pathway.

## Introduction

According to the Centers for Disease Control (CDC), The SARS-CoV-2 virus, or COVID-19, is responsible for 6,622,268 patient hospitalizations and 1,163,040 deaths as of December 23rd, 2023. Typically transmitted through respiratory droplets, the COVID-19 pandemic strained healthcare systems in most countries leading to significant economic losses. COVID-19 has an average incubation period of 6.4 days, and most patients experience symptoms of fever, cough, fatigue, and dyspnea . As the disease progresses, patients are at increased risk of suffering from a “cytokine storm”. Cytokines such as interleukins (ILs), interferons (IFNs), colony-stimulating factors (CSF), and tumor necrosis factors (TNFs), among many others, induce the inflammation cascade causing these cytokine storms. While the pathogenesis of a cytokine storm is not fully understood, it is known to be caused by various bacterial or viral infections, rheumatic conditions, sepsis, or drugs that cause an immune response. Pathogens invade the body starting the body’s innate immunity first. Infected epithelial cells release IL-1B and IFN-a/B, which in turn stimulate the natural killer (NK) cells. IFN-y, activated by IFN-a/B activates macrophages and releases large amounts of cytokines TNF-a and IL-12, which then activate the NK cells . This creates positive feedback between the macrophages and NK cells significantly increasing cytokine levels. Cytokines both promote and restrict each other to control the proliferation and differentiation of cells and regulate the inflammatory and immune responses during disease processes

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## Statement of the Problem

Until recently, symptomatic care was the protocol for patients infected with COVID-19. The use of oxygen for mild hypoxia and antipyretics for fevers was considered the standard of care (SOC). The use of antiviral medications, such as monoclonal antibodies, has been proposed in the treatment of acute COVID-19 infection. Many monoclonal antibodies are known inhibitors of cytokines, which are involved in the inflammatory process, whereas symptomatic care treats patients on a more superficial level.

## Research Question

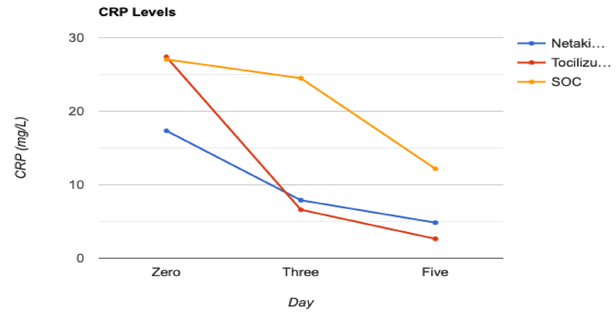
In patients who have been hospitalized for COVID-19, will treatment with monoclonal antibodies decrease mortality risk as opposed to symptomatic care alone?

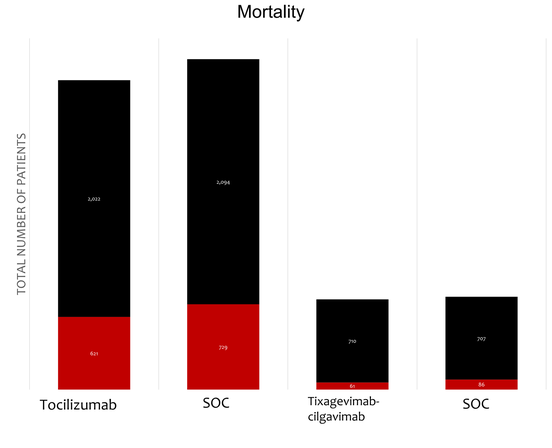
## Literature Review

- Patients who received Netakimab had a baseline average CRP level of 113 mg/L and showed a significant decrease in an average CRP of 29 mg/L at day three of treatment when compared to patients who received standard of care (SOC) (Avdeev et al., 2021).
- Patients who received netakimab had a baseline average CRP of 17.34 mg/L, which had decreased to 7.89 mg/L by day three and 4.84 mg/L by day five (Bryushkova et al., 2022).
- Patients who received netakimab group showed a significant reduction in LDH. The average LDH in the netakimab group was 247.6 U/L on day zero and had decreased to 210 U/L by day three (Bryushkova et al., 2022).
- 152 patients who received infusions of lenzilumab achieved survival without ventilation, as opposed to 144 SOC patients with baseline CRP levels of less than 150 mg/L (Temesgen et al., 2023) .
- Incidence of ECMO, IMV, or death was not statistically improved by lenzilumab in the overall patient population but was less likely when patients had a baseline CRP <150 mg/L (Temesgen et al., 2023).
- Patients who received tocilizumab combined with hydroxychloroquine had a baseline average CRP of 97 mg/dL with an endpoint average of 26 mg/dL (Sarhan et al., 2022).
- Patients who received tocilizumab showed a significant reduction in 28-day mortality as well as a significantly reduced the risk of progression to invasive mechanical ventilation (RCG, 2021).
- Patients who received tocilizumab combined with hydroxychloroquine had a baseline average LDH of 516 IU/L with an average endpoint average LDH of 312 IU/L (Sarhan et al., 2022).
- Patients who received garadacimab had no significant difference in the proportion of patients who progressed to endotracheal intubation or death when compared to patients receiving SOC treatment (Papi et al., 2023).
- Patients did not show a significant difference in incidence of invasive mechanical ventilation, admission to the intensive care unit (ICU), or mortality rate when compared to patients receiving SOC treatment (Fakharian et al., 2021).
- Patients who received tixagevimab-cilgavimab showed a significant decrease in mortality when compared to patients who received SOC treatment (TICO, 2022).

## Discussion

Based on the literature review, it can be determined that there is a benefit to using certain monoclonal antibodies in the treatment of COVID-19 when compared to SOC. There are three common goals throughout most of the studies regarding the use of monoclonal antibodies in patients with COVID-19. The first goal is to decrease the length of hospital admission, the second is to decrease the severity of symptoms that may be lethal to more fragile patients, and the third is to reduce the overall mortality of COVID-19. The true efficacy of monoclonal antibodies is difficult to determine due to SOC treatments differing across facilities. It is also difficult to determine if patients who were part of much larger and longer trials benefitted from the treatments from previous trials vs. the trials where monoclonal antibodies were used alone. Of the studies analyzed in the literature review, inflammatory markers showed significant decreases in patients who received netakimab, lenzilumab, and tocilizumab. Tocilizumab and netakimab were associated with a lower mortality rate when compared to all other monoclonal antibodies in the literature review. Netakimab, tocilizumab, lenzilumab, and tixagevimab-cilgavimab showed greater efficacy in decreasing the length of hospital stay and a decrease in overall mortality. Garadacimab was shown to be ineffective in decreasing mortality rate, length of hospital admission, and decreasing the incidence of patients requiring either CPAP or BiPAP. Adalimumab did not show a decrease in the length of hospital admission or a decrease in the likelihood of ICU admission (Fakharian et al.). The number and severity of adverse events recorded were shown to be similar across all trials of monoclonal antibodies when compared to standard-of-care treatment.




## Applicability to Clinical Practice

While this project focuses on the use of monoclonal antibodies on patients admitted to the hospital, there could be a potential for these infusions to be performed as an outpatient procedure in the clinic. These monoclonal antibody infusions could be administered to patients who do not meet the criteria for hospitalization but are still considered at high risk of severe disease progression. Outpatient monoclonal antibody infusions would use fewer resources than hospital admission and could lower the cost to the patient significantly. The studies have shown the risk of severe adverse reactions is low and the severity of the disease has also become reduced with certain monoclonal antibodies. If resources allow, patients could also potentially receive monoclonal antibody infusions in their own homes. Community Paramedics and Home Health Nurses can administer these infusions and monitor patients for adverse reactions. Having these infusions as outpatient procedures could reduce the rate of hospital admissions as well as lower the risk of spreading the infection to other patients and providers. Medical providers should continue to encourage high-risk patients to receive the COVID-19 vaccine as well as practicing proper handwashing and disease prevention.

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