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Tixagevimab and Cilgavimab: Can we see More Recommendations for Monoclonal Antibodies Beyond COVID-19 Vaccination

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Letter to the Editor

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Abstract

Nearly 3 years after its detection, the coronavirus disease 2019 (COVID-19) which is caused by severe acute respiratory syndrome CoV-2, is still a life-threatening global pandemic that has contributed to a high progression and mortality rate across the globe. This imposes the need for scientific research efforts in order to hold intense interest directed towards such exploration, for the development and optimization of different interventions to the COVID-19 infection. This commentary summarizes the potential clinical benefits for the recently authorized immunotherapy combination of Tixagevimab and Cilgavimab monoclonal antibodies for the prevention and treatment of COVID-19.

It is thought that about 2% of the global population is at increased risk of an inadequate response to COVID-19 vaccines and could benefit from pre-exposure prophylaxis. This particularly refers to patients with co-morbid disease conditions such as cardiovascular, respiratory, and endocrine disorders; as well as immunocompromised patients.[1] Currently, the clinically authorized monoclonal antibodies (mAbs) by the US FDA and European Medicines Agency (EMA) are a combination of Bamlanivimab plus Etesevima which was found to reduce the risk of COVID-19 hospitalization or death by 1%, a combined Casirivimab plus Imdevimab which was found to reduce the COVID-19 related hospitalization or deaths in high-risk patients by about 70%, and Sotrovimab.[2,3] The Alpha variant remains susceptible to all these mAbs that are currently available. The Beta and Gamma variants are much less susceptible to Casirivimab, Bamlanivimab, and Etesevimab; but the Casirivimab plus Imdevimab combination remains powerfully neutralizing, as does Sotrovimab. The Delta variant is less susceptible to the Bamlanivimab-etesevimab combination, but has shown vulnerability to neutralization by Sotrovimab and the Casirivimab plus Imdevimab combination.[4,5]

The recently FDA-approved mAbs is a combination of Tixagevimab and Cilgavimab by Astra Zeneca in December 2021. These are long-acting mAbs that neutralize all previous SARS-CoV-2 variants. They are specifically bound to different, non-overlapping sites on the spike protein of the SARS-CoV-2, and block virus attachment, and entry into human cells.[1] The pre-exposure prevention with this product achieved a statistically significant 77% reduction in the incidence of symptomatic COVID-19. This result was maintained for 6 months based on a randomized, double-blind, and placebo-controlled clinical trial. It is only authorized for adults and adolescents who are not currently infected with the novel coronavirus, and who have not recently been exposed to an infected individual. This combination is also characterized by 2 consecutive intramuscular injections, a different route of administration unlike the previous intravenous mAbs. However, the combination has also recorded incidents of hypersensitivity reactions with infrequent reports about serious cardiac events.[1,5]

In this light, patients who are not adequately protected by the COVID-19 vaccination will have an additional viable option for long-term protection through immunotherapy, thereby considerably reducing the risk of COVID-19 infection. Early mAbs treatment can reduce the risk of COVID-19 hospitalization and mortality rate in high-risk patients. However, even the recently approved mAbs combination by Astra Zenca, tixagevimab and cilgavimab, is considered not a substitute for COVID-19 vaccination.[1,3] More importantly, timing is critical in treatment by Tixagevimab and Cilgavimab. The earlier they are given, the more effective they are at treating or preventing COVID-19. Ideal time of treatment is within the first 4 to 5 days and not to be delayed more than 10 days after the onset of symptoms, with a gap duration of 90 days delay between mAbs treatment and vaccination in order to avoid any interference with the vaccine-induced immune responses.[1]

This provides an insight into the current speculations on the effectiveness of mAbs in the treatment of COVID-19. Literature relating to this topic is rapidly growing as these interventions would be a complement to the vaccines, while offering immediate protection upon administration that could last for months. The current therapeutic approaches would help reduce the risk and severity, all while mitigating the negative effects of COVID-19 complications.

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Conflicts of interest. The author declares no conflicts of interest.

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