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Mini Review

Monoclonal Antibodies In Covid-19: A Brief Insight

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Abstract

An outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first seen in Wuhan, China in December 2019. At the beginning of the pandemic, there was no drug which could be validated to be used to fight this deadly virus, but two years down the line, the armenaterium of drugs comprises of hydroxychloroquine, antivirals alone or in combination, antibiotics like azithromycin and doxycycline and low dose corticosteroids, either oral or intravenous. On the other hand, monoclonal antibodies have also played a significant role and have proved to be very effective in some cases. Here the authors have attempted to summate the role of new monoclonal antibodies and their effectiveness keeping in mind the discovery of the new variants of COVID-19.

Keywords: COVID-19; Monoclonal antibodies;

Introduction

Monoclonal antibodies (mAbs) are man-made proteins in the laboratory that act like human antibodies in the immune system. Various types of monoclonal antibodies exist and each monoclonal antibody is manufactured so that it binds to only one antigen. These are aimed in such a manner so that they identify and bind to precise receptors found on the surface of cells. These mimic the immune system's ability to fight off harmful pathogens such as viruses and cancer [1].

The genomic structure of SARS-CoV-2 consists of 4 structural proteins namely the spike (S), envelope (E), membrane (M), and nucleocapsid (N). The S1 subunit attaches to the angiotensin-converting enzyme 2 (ACE2) through its receptor-binding domain (RBD), initiating a change in S2 that results in virus-host cell membrane fusion and viral entry [2,3]. It has been proved that these anti-SARS-CoV-2 monoclonal antibodies (mAbs) targeting the spike protein are beneficial in treating SARS-CoV-2 infection [4,5].

Anti-SARS-CoV-2 mAbs that have received EUA from the FDA

At present, three anti-SARS-CoV-2 mAbs have been given Emergency Authorizations for the treatment of mild to moderate COVID-19 infections in non-hospitalized patients who are at high risk for progressing to severe disease. These products are:

- **Bamlanivimab plus Etesevimab**: Neutralizing mAbs that bind to different, but overlapping, epitopes in the spike protein RBD of SARS-CoV-2. It is authorized for adults and children of all ages, including infants and neonates.

- **Casirivimab plus Imdevimab**: Recombinant human mAbs that bind to nonoverlapping epitopes of the spike protein RBD of SARS-CoV-2.

- **Sotrovimab:** It targets an epitope in the RBD of the spike protein that is conserved between SARS-CoV and SARS-CoV-2 [6].

Indications, Administration and Dosage of Anti-SARS-CoV-2 mAbs

Treatment should be started immediately on obtaining a positive result of SARS-CoV-2 antigen test or nucleic acid amplification test (NAAT) and within 10 days of symptom onset [7]. At present, it has not been advocated for use in hospitalized patients with severe COVID-19; however, they may be available through expanded access programs for patients who either have not developed an antibody response to SARS-CoV-2 infection or are not expected to mount an effective immune response to infection.

- Bamlanivimab 700 mg plus Etesevimab 1,400 mg (or weight-based dosing for pediatric patients weighing <40 kg) administered as an intravenous (IV) infusion [8].

- Casirivimab 600 mg plus Imdevimab 600 mg administered as an IV infusion. If an IV infusion is not feasible or would cause a delay in treatment, these can be administered as 4 SQ injections (2.5 mL per injection)

- Sotrovimab 500 mg administered as an IV infusion.

Recommendations

The recommendations for the use of anti-SARS-CoV-2 mAbs as treatment are based on the FDA EUA criteria for the following conditions and other factors. Medical Conditions or other factors that were represented in patients in clinical trials [7].

- Aged ≥65 years
- Obesity (BMI >30 Kg/M^2)
- Diabetes
- Cardiovascular disease (including congenital heart disease) or hypertension
- Chronic obstructive pulmonary disease, moderate-to-severe asthma, interstitial lung disease, cystic fibrosis, pulmonary hypertension)
- Immuno compromising condition or immunosuppressive treatment
- Chronic kidney disease
- Pregnancy
- Sickle cell disease
- Neurodevelopmental disorders.

SARS-CoV-2 Variants to Anti-SARS-CoV-2 mAbs

With the advent of several new mutations in the SARS-CoV-2 genome and discovery of several novel variants, there has been a marked reduction in the susceptibility to a number of the authorized anti-SARS-CoV-2 mAbs. The clinical relevance of reduced in vitro susceptibility of select variants to anti-SARS-CoV-2 mAbs is under investigation [8].

- **Alpha (B.1.1.7):** This variant retains in vitro susceptibility to all the anti-SARS-CoV-2 mAbs that are currently available through EUAs.

- **Beta (B.1.351):** *In vitro* studies suggest that the Beta variant has markedly reduced susceptibility to Casirivimab, although the combination of Casirivimab and Imdevimab appears to retain activity against the variant. Sotrovimab also appears to retain activity against the variant.

- **Gamma (P.1):** The Gamma variant also has reduced susceptibility to Casirivimab; however, the combination of Casirivimab plus Imdevimab appears to retain activity against the variant. Sotrovimab also appears to retain activity against the Gamma (P.1) variant.

- **Delta (B.1.617.2.):** This VOC retains in vitro susceptibility to all the anti-SARS-CoV-2 mAbs that are currently available through FDA EUAs.

- **Omicron (B.1.1.529):** Ongoing studies are evaluating the susceptibility of this VOC to the anti-SARS-CoV-2 mAbs. This variant, which includes numerous mutations in the spike protein, is predicted to have markedly reduced susceptibility to some anti-SARS-CoV-2 mAb products, including bamlanivimab plus etesevimab and casirivimab plus imdevimab. Sotrovimab appears to retain activity against this variant.

Genomic studies of the types of SARS-CoV-2 variants, as well as studies on the susceptibility of different variants to available anti-SARS-CoV-2 mAbs, will be important in defining the utility of specific mAbs in future.

Considerations in pregnancy

The use of anti-SARS-CoV-2 mAbs can be considered for pregnant people with COVID-19, especially those who have additional risk factors for severe disease. As immunoglobulin (Ig) G mAbs, the authorized anti-SARS-CoV-2 mAbs would be expected to cross the placenta. There are no pregnancy-specific data on the use of these mAbs; however, other IgG products have been safely used in pregnant people when their use is indicated. Therefore, authorized anti-SARS-CoV-2 mAbs should not be withheld in the setting of pregnancy.

Considerations in children

Although EUAs have been issued for Bamlanivimab plus Etesevimab and Casirivimab plus Imdevimab for the treatment of non-hospitalized, high-risk patients aged ≥12 years and weighing ≥40 kg with mild to moderate COVID-19, there are currently no data available to determine which high-risk pediatric patients defined in the EUAs will likely benefit from these therapies. In consultation with a pediatric infectious disease specialist, Bamlanivimab plus Etesevimab or Casirivimab plus Imdevimab can be considered on a case-by-case basis for children who meet the EUA criteria, but should not be considered routine care. There are currently no data to support the use of anti-SARS-CoV-2 monoclonal antibodies in hospitalized children for COVID-19.

Anti-SARS-CoV-2 mAbs and COVID-19 vaccination

For people who have received anti-SARS-CoV-2 mAbs for treatment, COVID-19 vaccination be deferred until at least three months after therapy. For people who have received anti-SARS-CoV-2 mAbs for PEP, vaccination should be deferred until at least 30 days after PEP. These deferrals are precautionary because of the theoretic possibility that anti-SARS-CoV-2 mAb treatment may interfere with vaccine-induced immune responses.

For people who develop COVID-19 after vaccination, if there are no logistical or supply constraints limiting the availability of the authorized anti-SARS-CoV-2 mAbs, prior vaccination should not affect decisions regarding the use and timing of anti-SARS-CoV-2 mAb treatment.

Adverse effects and monitoring

The authorized anti-SARS-CoV-2 mAbs should be administered by IV infusion or SQ injections and should only be administered in health care settings by qualified health care providers who have immediate access to emergency medical services and medications that treat severe infusion-related reactions. Patients should be monitored during the IV infusion or SQ injections and for at least 1 hour after the infusion or injections are completed. Hypersensitivity, including anaphylaxis and infusion-related reactions, has been reported in patients who received anti-SARS-CoV-2 mAbs. Rash, diarrhea, nausea, dizziness, and pruritis have also been reported. Injection site reactions, including ecchymosis and erythema, were reported in clinical trial participants who received casirivimab plus imdevimab by SQ administration.

Drug-drug interactions

Drug-drug interactions are unlikely between the authorized anti-SARS-CoV-2 mAbs and medications that are renally excreted or that are cytochrome P450 substrates, inhibitors, or inducers.

Conclusion

The pandemic is still in full flow and despite the massive immunization coverage been done in the entire world, the hospitals are still overwhelmed with patients of COVID-19. The different modalities of treatment have seen a vast change since the first day and with the rapid rate at which the new variants of SARS-CoV-2 are being discovered, the need of the hour is to update and modify the pre-existing treatment modules. The monoclonal antibody therapy was a huge success and proved to be effective in several cases and with the entry of newer drugs, we have even seen a better efficacy.

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