Research & Reviews in Biotechnology & Biosciences **ISSN No: 2321-8681**
Website: www.biotechjournal.in **Mini-Review**
Volume: 9, Issue: 1, Year: 2022 **PP: 85.92**
DOI: https://doi.org/10.5281/zenodo.6620700 **Peer Reviewed Journal**

Review On Mab's boon for Covid – 19

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Article History

Received: 26/03/2022
Accepted: 02/04/2022

Article ID: RRBB/126

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Abstract:

Covid 19 virus called severe acute respiratory syndrome (SARS-CoV-2) contains spike proteins that assist the virus in entering host cells. Scientific community from the entire world is working to find an effective treatment for SARS-CoV-2. By using modern biotechnology treatment, monoclonal antibodies (MAbs) are being designed and developed to block a particular pathway of SARS-CoV-2 infection.. Many of them target the receptor binding protein so that the interaction between virus and host cell can be prevented. These prepared monoclonal antibodies are currently preferred for high-risk patients such as those over 65 years old with compromised immunity and those with metabolic disorders such as obesity. Being highly specific in action, monoclonal antibodies offer one of the most appropriate interventions for both the prevention and treatment of SARS-CoV-2. Although Monoclonal antibodies are specific in action but are also known to induce immunogenic and non-immunogenic reactions. More research and testing are required to establish the suitability of administering MAbs to all patients at risk of developing a severe illness. This is review study is focused on MAbs as a therapeutic option for treating COVID-19, as well as their discovery, mechanism of action, and key characteristics.

Keywords:"Covid 19". "Monoclonal antibody", "pneumonia "

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Introduction

A sudden rise of pneumonia of unknown pathology in Wuhan City of China emerged in December 2019. Later on after studies novel virus called corona virus was identified as the causative agent and was subsequently termed COVID-19 by the World Health Organization (WHO) . The infection rapidly spread to different parts of the world and by the World Health Organization (WHO) in March 2020 declared it as a pandemic. Pandemic has resulted in more than 4.7 million deaths globally and nearly 227 million cases, main challenge on health professionals and scientist is to prevent the infection and treatment research. The deadly corona virus belongs to the large family of beta-corona virus and is named as (SARS-CoV-2) Severe Acute Respiratory Syndrome. The virus is being mutated at regular intervals, and some of the variants have been found to be more virulent and resistant to certain vaccines. The patients suffering with covid 19 infection bears symptoms of dry cough, dyspnea, fever, bilateral lung infection. However, some have developed various fatal complications including organ failure, septic shock, even death too. 60% of those infected with covid – 19 are male with a median age of 55 years. A majority of patients in over 75% of patients, the disease is characterized by mild symptoms, such as throat infection, cough, fever, and difficult breathing. However remaining 25% of patients include aged people, immuno compromised and co-morbid patients, the infection can cause severe lung infections such as pneumonia, pulmonary edema, acute respiratory syndrome, it may also cause, multi organ failure and death too. Symptomatic diagnosis of COVID-19 is difficult and is considered incorrect due to the resemblance to a common seasonal viral infection which includes symptoms like common cold caused by rhino virus. Suspected individuals should be diagnosed with (RT-PCR) real-time polymerase chain reaction by collecting samples from nasal and throat swabs for confirming the infection. The nuclear component of SARS-CoV-2 is a beta-corona virus containing RNA as genetic material. The genetic sequencing found that the virus has 96% nuclear similarity with bat. (Asda, 2021)

Current therapeutic options to treat COVID-19

Sr. No.	Class	Examples
1.	Protease inhibitors	Scutellarin , quercetagetin , myricetin and robinetin
2.	Non-structural proteins inhibitor	Aryl diketoacids
3.	Peptides	Thymosin α1 peptide
4.	RNA products	Soluble ACE2 in DNA encoding form
5.	Vaccines	Vector-based and attenuated vaccines by intra-nasal route
6.	Inhibitors of unknown target	Amiodarone, Dronedarone, mono-desethyl-amiodarone

Monoclonal antibodies (MAbs) are one of the emerging therapeutic agents used to SARS COV-2. They are one of the rapid growing therapeutic agents and are considered to be highly specific in their action and specific towards target too. Monoclonal antibodies (MAbs) are lab-grown antibodies that act on single target,

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causing its destruction immediately. Normally, Monoclonal antibodies (MAbs) are produced by B cells in patients after several days of infection. They also can be synthesized in the laboratory by immunizing animals such as mice and they can also be constructed by molecular engineering. Monoclonal antibodies (MAbs) are gaining popularity among physicians as well as in patients because these agents are known to act on fixed target and at specific site only (Reka1, 2021).

Material & Methods

A review of the latest literature until December, 2021 was made. Studies published in English and available as full-text publications are included. The data was collected from the E journals like Scopus , web of science and Google Scholar platforms using the following keywords: "SARS-COV2", "corona virus " , "monoclonal antibodies". Original and review papers were referred too, whereas letters to the editor and preprints were excluded. After reading abstracts, 15 papers that met the adopted criteria, were selected for analysis

Description of Monoclonal Antibodies

In 1975, Kohler and Milstein demonstrated a new technology to isolate single specific targeted antibodies called Monoclonal Antibodies. Most of them are used for cancer therapy, but many of newer MAbs are being tested and approved for treating other diseases. (Asda, 2021). These antibodies possess a common antigen recognition site, affinity, biological interaction, and similar physiological effects. Monoclonal antibodies differs from Polyclonal antibodies by as they are produced by the immune system and are usually polyclonal, i.e., produced by different B lymphocytes. Multifunctional immunoglobulins/antibodies are considered multifunctional since they show numerous cellular and humeral reactions to antigens.

A brief summary of the MAbs developed through different mechanisms is represented in Table

Sr. No.	Technical Design	Examples
1.	Hybridoma	Muromonab Abciximab Palivizumab
2.	Phage display	Adalimumab Moxetumomab
3.	Transgenic mice	Panitumumab Ustekinumab Alirocumab

Discussion

After full speed of COVID-19 pandemic, hospitality and mortality resulting from severe SARS-CoV-2 infection remain high. Therapeutic approaches target with the help of antiviral drugs or many of used as immune boosters. A group of world scientist are trying their best attempt to develop and rapidly distribute effective vaccines against SARS-CoV-2. But huge number of doses are required to vaccinate peoples around the globe. Meanwhile, attention has been focused on monoclonal antibodies capable of blocking the interaction between viral proteins and human cells. Monoclonal antibodies are intended to target a particular infection process, and this makes them

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distinct from other chemotherapy. The main goal of SARS-CoV-2 monoclonal antibodies is surface spike glycoprotein's, the key elements that get the virus into the target cells . In severely and critically ill SARS-CoV-2 infected patients there is often a adverse immune response, usually referred as cytokine release storm (CRS), characterized by high levels of inflammatory markers, like C-reactive proteins, Interleukin-6, ferritin and lactate dehydrogenase. Available data suggest that the administration of MAbs that lower the levels of cytokine, reducing the risk of CRS, this could lead to a clinical benefit, reducing mortality rate from COVID-19 . Clinically, the combination of monoclonal antibodies like casirivimab and imdevimab or bamlanivimab reduced the hospitalization rate and emergency department admissions in patients with a mild infection, and risk factors for severe manifestation from COVID-19 these results, the FDA and EMA released a EUA for both the combination of casirivimab and imdevimab and bamlanivimab for mild symptomatic adults with COVID-19 who are not in need of additional oxygen but are at high risk of becoming severely ill. However, monoclonal antibodies are expected to work better in the early infective phase of SARS-CoV2 infection. MAbs of SARS-CoV-2. Monoclonal antibodies like Bamlanivimab: Bamlanivimab, [LY3819253]' [LYCoV555] , is a neutralizing Mab that binds to the RBD of the S protein of SARS-CoV-19 . A randomized controlled phase I/II trial (BLAZE-1 study) compared bamlanivimab (three doses: 700, 2800, and 7000mg) with placebo.103 the primary outcome was SARS-CoV-2 virus load reduction from day 1 to day 11. The results showed that antibody induced by 2800-mg dose experienced significant decrease than that induced by placebo. Meanwhile, the 700- and 7000-mg groups had no tendency of notable reduction, possibly because these patients had been effectively cleared from SARS-CoV-2 before day 11. The most common adverse event of bamlanivimab was nausea (3.9%), followed by dizziness (3.2%) and moderate infusion responses (2.3%). Bamlanivimab showed decreased severity of symptoms and hospitalization proportion compared with the placebo group. On November 10, 2020, bamlanivimab was issued EUA for patients with mild-to moderate COVID-19 (pediatric and adults). The authorized administration is the single 700-mg dose with vein injection infusion for >60min.

Bamlanivimab combination with etesevimab: Bamlanivimab and etesevimab (LY-CoV016) are neutralizing MAbs that target different but overlapping epitopes in the RBD of the S protein of SARS-CoV2. A randomized controlled phase III trial (BLAZE-1 study) included >1000 participants and compared bamlanivimab plus etesevimab with placebo.107,108 The results suggested that the participants who received bamlanivimab plus etesevimab had a 70% relative reduction and a 5% absolute reduction in Covid-19related hospitalizations or death from any cause compared with those in the placebo group ($p<0.001$). Endpoint events occurred in 2% of the participants in the bamlanivimab plus etesevimab group and 7% in the placebo group. The BLAZE-4 trial focused on the dose of bamlanivimab and etesevimab.107 Furthermore, the FDA selected

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bamlanivimab 700mg and etesevimab 1400mg to be the authorized dose for patients with mild-to-moderate COVID-19.109 this dosage was subsequently studied in a new BLAZE-1 trial. The bamlanivimab and etesevimab group also showed superior death and hospitalization rate than the placebo group. On March 5, 2021, the European Medicines Agency has allowed EU Member States to utilize bamlanivimab plus etesevimab for emergency use in patients with COVID-19.

Conclusions

The present study reviewed the development of monoclonal antibodies. Advanced techniques that helped us in understanding the pathophysiology and behavior of SARS-CoV-2 infection as well as the key biomolecules like enzymes and proteins necessary for its replication. Highly specific in their target and specific in action, monoclonal antibodies are designed and developed to attack one or more sites of viral pathogenesis. The number of the registered patents for monoclonal antibodies targets the Spike protein and its binding sites. Considering the current situation where SARS-CoV-2 is being mutated at very regular intervals, more aggressive approaches, such as the combination of monoclonal antibodies with other known therapeutic interventions, need to be evaluated clinically to win the battle against COVID-19 infection and to conclude the pandemic.

Provenance and peer review

Not commissioned, internally peer-reviewed.

Sources of funding

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Author contribution

Kale Rohit: Conceptualization, Data study, Visualization, Writing - Original Draft, Writing - review & editing..

Solanke Shrikant: Data study, Visualization

Declaration of conflict of interest

All authors report no conflicts of interest relevant to this article.

Acknowledgements

All the authors acknowledge and thank their respective Universities and Institutes.

Ethical statement

Not applicable

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