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Review Article

Monoclonal Antibodies for Treatment of COVID-19: An Updated Review of Current Evidence

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Abstract

The emergence of COVID-19 in December 2019 spurred a global effort to develop effective medical interventions. Therapeutic monoclonal antibodies (mAbs) have emerged as a promising strategy to combat the SARS-CoV-2 virus. Several mAbs targeting the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein have received Emergency Use Authorization (EUA) for treating mild to moderate COVID-19. Additionally, human mAbs and hyperimmune plasma derived from recovered COVID-19 patients have been explored as potential therapeutic options. This review delves into the potential of mAbs for the diagnosis and treatment of COVID-19 infection. We discuss the mechanisms of action of mAbs, as well as their advantages and limitations. Furthermore, we explore the ongoing research and development efforts to optimize mAb-based therapies for COVID-19.

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INTRODUCTION

The COVID-19 pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in Wuhan, China, in December 2019 and rapidly spread globally. This pandemic has resulted in millions of infections and deaths worldwide. SARS-CoV-2 is an enveloped, positive-sense single-stranded RNA virus belonging to the Betacoronavirus genus[1,2]. Its large genome encodes both structural and non-structural proteins, including the spike (S) protein, which plays a crucial role in viral entry into host cells[3].

The S-protein is a prime target for therapeutic intervention, as it is essential for viral attachment and entry. Neutralizing monoclonal antibodies (mAbs) that bind to the S-protein can effectively block viral infection[4]. While significant efforts have been directed towards vaccine development and antiviral therapies, the potential of mAbs as a therapeutic strategy against COVID-19 has gained increasing attention[5]. Monoclonal antibodies can offer several advantages, including rapid onset of action, high specificity, and the potential to target multiple viral epitopes. However, their therapeutic use is often limited by factors such as cost, production complexity, and potential for immunogenicity[6].

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Understanding the complex interplay between the virus and the host immune response is crucial for developing effective therapeutic strategies[7]. In the early stages of COVID-19 infection, antiviral therapies like remdesivir can be beneficial in reducing viral replication. However, as the disease progresses, the host immune response can contribute to severe disease outcomes[8,9]. In such cases, immunomodulatory therapies, such as corticosteroids and interleukin-6 inhibitors, can help mitigate the inflammatory response[10].

The COVID-19 pandemic has underscored the urgent need for innovative therapeutic approaches to combat this highly contagious disease[11]. Monoclonal antibodies have emerged as a promising therapeutic strategy due to their ability to target specific viral proteins and neutralize the virus. Given the ongoing threat of COVID-19 and the emergence of new variants, continued research into the development of novel therapeutic strategies, including mAb-based therapies, is essential[12,13]. This review will explore the development and clinical application of various mAb therapies for COVID-19, providing an overview of their mechanisms of action, efficacy, and safety profiles.

MONOCLONAL ANTIBODIES

Monoclonal antibodies are laboratory-produced antibodies designed to mimic the immune system's ability to fight off harmful antigens. They are typically derived from either convalescent human B-cell lymphocytes or humanized mice. By cloning a single antibody, scientists can produce a large quantity of identical antibodies with high specificity for a particular target antigen[14,15]. Monoclonal antibody therapies have emerged as a promising approach to treat COVID-19. By targeting specific viral proteins, these therapies can help prevent severe illness, reduce viral load, and mitigate symptoms[13,16]. However, it's important to note that mAb therapy is not a substitute for vaccination. Vaccination remains crucial for building herd immunity and preventing the spread of the virus[17]. There are four primary methods for producing mAbs, each with distinct characteristics.

Murine Antibodies

Murine antibodies are derived from mouse proteins and are identified by names ending in "-omab"[18]. For instance, muromonab, the mAb anti-CD3 antibody used as immunosuppressive therapy in kidney, heart, and liver transplant patients[19].

Chimeric Antibodies

Chimeric antibodies are a class of monoclonal antibodies that combine human and mouse antibody sequences. This hybrid approach aims to reduce immunogenicity while maintaining therapeutic efficacy[20]. Chimeric antibodies are named with the suffix "-ximab"[18]. For instance, infliximab is a chimeric antibody approved for the treatment of various inflammatory conditions, including rheumatoid arthritis, inflammatory bowel disease, and ankylosing spondylitis[21].

Humanized Antibodies

Humanized antibodies are a class of therapeutic antibodies that combine the specificity of mouse antibodies with the safety profile of human antibodies. These antibodies are engineered to have a human-like framework, reducing the risk of immunogenicity and improving their therapeutic potential[20]. The names of many humanized antibody drugs end in "-zumab"[18]. For instance, trastuzumab is a well-known humanized monoclonal antibody used to treat certain types of breast, stomach, and gastroesophageal junction cancers[22].

Human Antibodies

Human antibodies, named with the suffix "-umab"[18], are therapeutic proteins derived from human immune cells. These antibodies are engineered to bind specifically to target molecules involved in disease processes[20]. Adalimumab, a well-known example, is a monoclonal antibody that targets tumor necrosis factor-alpha (TNF-α), a key inflammatory cytokine. This targeted approach offers several advantages, including reduced immunogenicity and increased efficacy compared to traditional antibody-based therapies[23].

ANTI-SARS-COV-2 MONOCLONAL ANTIBODIES

The SARS-CoV-2 genome encodes four major structural proteins: spike (S), envelope (E), membrane (M), and nucleocapsid (N). Additionally, several non-structural and accessory proteins are also expressed[24]. The S-protein, composed of S1 and S2 subunits, plays a crucial role in viral entry. The S1 subunit binds to the human angiotensin-converting enzyme 2 (ACE2) receptor, facilitating viral attachment to host cells. Subsequently, the S2 subunit undergoes conformational changes, triggering membrane fusion and viral entry[25-27].

Anti-SARS-CoV-2 mAbs targeting S-protein have demonstrated clinical efficacy in managing SARS-CoV-2 infections. These mAbs have been successfully used for post-exposure prophylaxis in individuals exposed to the virus in residential settings. Additionally, they have been employed in specialist and home care settings during outbreaks[28]. Furthermore, pre-exposure prophylaxis with certain anti-SARS-CoV-2 mAbs has been shown to significantly reduce the risk of infection[29].

The development of mAbs has emerged as a promising strategy for the diagnosis and treatment of COVID-19. Several pharmaceutical companies, including Celltrion, AstraZeneca, and Regeneron, have actively pursued the development of mAbs targeting the SARS-CoV-2 virus. The U.S. Food and Drug Administration (FDA) has granted emergency use authorization (EUA) to several mAb therapies, such as bamlanivimab, a combination therapy of bamlanivimab and etesevimab, casirivimab and imdevimab, and sotrovimab, for the treatment of mild to moderate COVID-19 in high-risk individuals[30]. While mAbs have shown promise in combating COVID-19, the emergence of SARS-CoV-2 variants with mutations that reduce susceptibility to these therapies poses a significant challenge. Additionally, the development of mAb therapies for other viral diseases, such as Ebola virus disease, has demonstrated the potential of this approach in addressing infectious diseases[31].

Bamlanivimab

Bamlanivimab, the mAb specifically designed to block the SARS-CoV-2 spike protein from binding to the human ACE2 receptor, was granted EUA by the FDA on November 9, 2020, for the treatment of mild to moderate COVID-19 in high-risk adult and pediatric patients[32]. Administered as a single 700 mg infusion, bamlanivimab was the first mAb approved for COVID-19 treatment. However, subsequent studies revealed limited efficacy in reducing viral load. Consequently, the FDA revoked the EUA for bamlanivimab monotherapy on April 16, 2021, citing the emergence of SARS-CoV-2 variants resistant to this therapy (**Figure 1**)[33].

Casirivimab and Imdevimab Combination

The R10933-10987-COV-2067 Phase III trial evaluated the efficacy of casirivimab and imdevimab in treating mild to moderate COVID-19 infection[34,35]. Following EUA by the FDA on November 21, 2020, this antibody cocktail, marketed as Regeneron's REGN-COV2, was administered via intravenous infusion or subcutaneous injection. The treatment involves a combination of 600 mg casirivimab and 600 mg imdevimab, targeting non-overlapping epitopes of the SARS-CoV-2 spike protein[36]. However, due to the emergence of the Omicron variant, which exhibits reduced susceptibility to these antibodies, the distribution of casirivimab and imdevimab in the United States has been suspended. Individuals infected with the Omicron variant are unlikely to benefit from this treatment[37].

The clinical studies are evaluating the efficacy of REGN-COV2 in several populations. Firstly, the drug is being tested in adolescents aged 12 and older to assess its ability to alleviate COVID-19 symptoms. Secondly, its effectiveness in reducing viral load in children under 18 years of age is being explored. Additionally, the study is comparing the efficacy of REGN-COV2 to placebo in hospitalized patients with mild to moderate COVID-19, focusing on factors such as survival rates and the need for mechanical ventilation[38,39]. Notably, patients treated with the cocktail did not require hospitalization due to COVID-19 within a 41-day observation period[40].

REGN-COV2 has shown significant promise in combating COVID-19. Clinical trials have demonstrated a 70% reduction in hospitalization and mortality rates among high-risk individuals. Additionally, when administered to individuals exposed to the virus, REGN-COV2 can reduce the risk of symptomatic infection by 80%[13], as shown in **Figure 1**. Notably, individuals with no pre-existing SARS-CoV-2 antibodies experienced the greatest clinical benefit.

Bamlanivimab and Etesevimab Combination

Bamlanivimab and etesevimab, a combination of monoclonal antibodies, target multiple epitopes on the SARS-CoV-2 spike protein. This dual-antibody approach aims to neutralize the virus and prevent its entry into human cells[41]. On February 9, 2021, the FDA granted EUA for this combination therapy to treat mild to moderate COVID-19 in non-hospitalized pediatric patients. By binding to the receptor-binding domain of the spike protein, these antibodies effectively block viral attachment and entry into host cells[30].

Initially, a combination therapy of bamlanivimab (700 mg) and etesevimab (1400 mg) was administered intravenously to individuals in regions with low levels of SARS-CoV-2 mutations. However, official guidelines advised against COVID-19 vaccination within three months of receiving this treatment[42]. A recent phase I clinical trial demonstrated a 70% reduction in COVID-19-related hospitalizations among patients who received bamlanivimab and etesevimab compared to placebo[43]. The distribution of bamlanivimab and etesevimab was temporarily suspended in the United States due to the emergence of the Omicron variant, which exhibits reduced susceptibility to these monoclonal antibodies. As a result, individuals infected with the Omicron variant are unlikely to benefit from this treatment[44]. The product's availability was reinstated as the prevalence of the Gamma and Beta variants declined to less than 5%. The US FDA and the European Medicines Agency (EMA) have recommended the use of monoclonal antibody (mAb) combinations, such as casirivimab and imdevimab (REGN-CoV-2) as well as bamlanivimab and etesevimab, for outpatients at high risk of severe COVID-19 who do not require supplemental oxygen therapy (**Figure 1**)[45].

Sotrovimab

Sotrovimab, the mAb initially discovered in a SARS-CoV survivor in 2003, targets a conserved epitope on the SARS-CoV-2 spike protein's RBD. It received EUA from the FDA in May 2021 for the treatment of mild-to-moderate COVID-19 in high-risk individuals[46]. Administered as a single 500 mg intravenous infusion, sotrovimab has demonstrated a significant reduction in hospitalizations and deaths compared to placebo. In a clinical trial involving 583 participants, only 1% of those treated with sotrovimab required hospitalization or died within 29 days, compared to 7% in the placebo group. This translates to a 6% absolute reduction and an 85% relative reduction in severe outcomes (**Figure 1**). While intravenous administration is the current standard, intramuscular formulations are under clinical investigation[47].

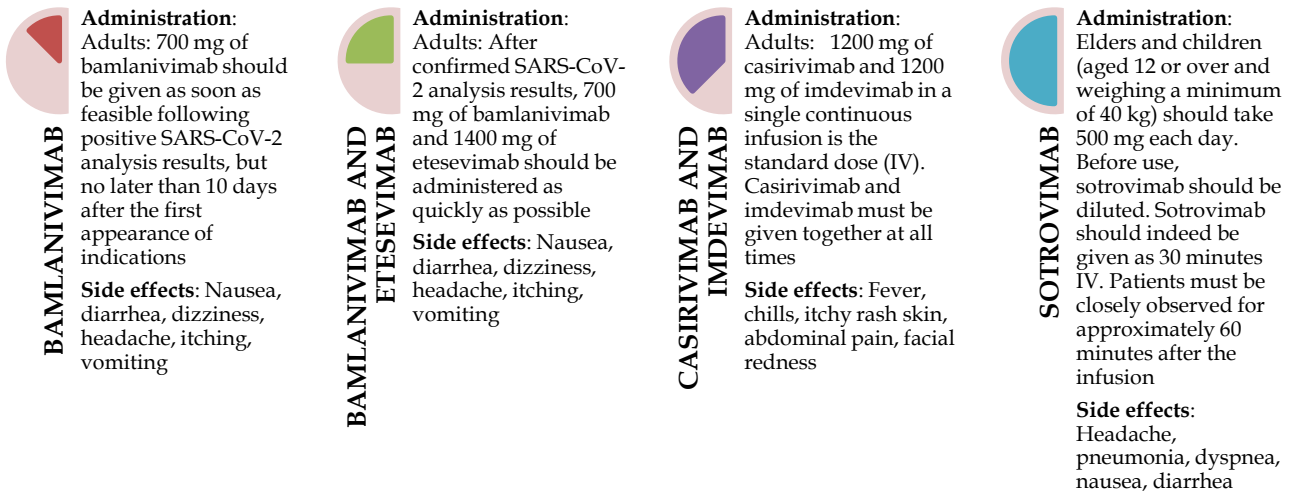

Figure 1. Administration information for mAbs currently approved for COVID-19 and their side effects.

MONOCLONAL ANTIBODIES INFUSION CRITERIA

The FDA EUAs for mAbs targeting SARS-CoV-2 outline specific criteria for individuals at increased risk of severe COVID-19. These criteria were expanded on May 14, 2021, to include individuals diagnosed with other medical conditions who

have mild to moderate COVID-19 and are at high risk of progressing to severe disease. However, the use of mAbs is not recommended for all COVID-19 patients[48,49].

The administration of mAbs is typically considered for individuals with mild to moderate COVID-19 who are at high risk of developing severe disease or hospitalization. This includes patients who have been hospitalized for reasons other than COVID-19 or those who meet specific eligibility criteria for outpatient treatment[50]. Importantly, mAbs are not recommended for patients with severe COVID-19 requiring oxygen therapy. To maximize the effectiveness of mAb treatment, it is crucial to initiate therapy as early as possible after symptom onset and within 10 days of a positive COVID-19 test[51]. Early administration allows mAbs to effectively neutralize the virus and prevent its replication. Beyond this 10-day window, the therapeutic benefit of mAbs diminishes significantly[52].

Patients should be monitored for at least one hour following intravenous or subcutaneous administration of mAb therapy. Additionally, current recommendations advise against receiving COVID-19 vaccination within three months of mAb treatment. This precautionary measure is implemented to prevent potential interference with vaccine-induced immune responses[53]. The Centers for Disease Control and Prevention (CDC) specifically recommends a 90-day interval between the first and second doses of COVID-19 vaccine for individuals who have received mAb therapy[54].

Individuals who are at high risk of severe COVID-19 infection may benefit from therapeutic interventions. This includes those who are unvaccinated or have compromised immune systems due to underlying health conditions or immunosuppressive medications. Additionally, individuals who have frequent close contact with COVID-19 patients may also be considered for therapeutic treatment[55].

High-Risk Conditions

Individuals 12 years and older are considered high-risk for severe COVID-19 if they meet at least one of the following criteria:

1. Age: 65 years or older
2. Obesity: BMI ≥25 kg/m² for adults, BMI ≥85th percentile for children aged 12-17
3. Pregnancy
4. Chronic kidney disease
5. Diabetes
6. Hypertension or cardiovascular disease
7. Chronic lung diseases (e.g., COPD, severe asthma, interstitial lung disease, cystic fibrosis, pulmonary hypertension)
8. Sickle cell disease
9. Neurological disorders (e.g., cerebral palsy)
10. Immunocompromising conditions (e.g., congenital immunodeficiencies, organ transplantation, HIV infection, cancer treatment)
11. Dependency on medical devices (e.g., tracheostomy, gastrostomy, ventilator)
12. Infants under 12 months

It's important to note that the presence of multiple high-risk conditions further increases the risk of severe COVID-19 infection[56].

Mechanism of Action

The SARS-CoV-2 virus relies on its spike protein to invade human cells. This crucial protein binds to the human ACE2 receptor, enabling the virus to enter and replicate. Neutralizing mAbs specifically target this spike protein, effectively blocking viral entry and preventing infection. By hindering the virus's ability to attach to host cells, these mAbs can significantly reduce the severity of COVID-19. The rapid progress in understanding the structure of the SARS-CoV-2 spike protein, aided by prior experience with other human viruses, has accelerated the development of effective mAb-based therapies[4,57].

To initiate infection, SARS-CoV-2 must first bind to the host cell surface receptor, ACE2, through its S-protein. This interaction is facilitated by the transmembrane protease serine 2 (TMPRSS2). Neutralizing mAbs can effectively block this initial step by binding to the S-protein, thereby preventing viral entry into the host cell. While most mAbs target the RBD of the S-protein, which is crucial for ACE2 binding, some mAbs may target other epitopes on the S-protein to achieve

neutralization. The potency of neutralizing antibodies, as demonstrated by previous studies on SARS-CoV and MERS-CoV, is a critical factor in determining their clinical potential[58].

Production

Monoclonal antibodies are produced by B lymphocytes and are essential tools in various biomedical applications. Traditionally, mAbs were generated from murine B cells, limiting their therapeutic potential due to immunogenicity. To overcome this challenge, techniques have been developed to produce mAbs in stable cell lines, including those derived from human B cells[59]. By utilizing human B cells, particularly from convalescent COVID-19 patients, researchers have successfully generated humanized mAbs that exhibit potent neutralizing activity against SARS-CoV-2. These humanized mAbs hold significant promise as therapeutic agents for COVID-19 and other infectious diseases[60].

Traditional production of mAbs in mice involves a multi-step process. First, mice are immunized with a specific antigen, such as the SARS-CoV-2 spike protein. Then, their spleen cells, which produce antibodies against the antigen, are fused with immortalized myeloma cells using a fusing agent like polyethylene glycol. This fusion creates hybridomas, which are cells that can continuously produce the desired mAbs. These hybridomas are then cloned and subcloned to obtain stable cell lines that produce a single type of mAb[61]. Historically, most mAbs produced using this method have been mouse mAbs, and many of these have been used in immunotherapy[62].

To generate recombinant human mAbs, the cDNA sequences encoding the variable regions of the heavy and light chains of interest must be cloned into expression plasmids. These plasmids typically contain the constant regions of human IgG1 heavy chain and Ig kappa light chain, along with a signal sequence (such as the interleukin-2 signal sequence) to facilitate efficient secretion of the recombinant antibody. Following transfection of mammalian cells, such as HEK-293T cells, with the expression plasmids, the recombinant human mAbs are produced and purified using protein A affinity chromatography[63].

Hybridoma technology, introduced in 1975, revolutionized the production of mAbs. By fusing immortalized myeloma cells with antibody-producing B cells, researchers can generate stable cell lines that produce large quantities of specific mAbs. This technique was employed to develop mouse mAbs targeting specific surface epitopes on the SARS-CoV S-protein. Subsequently, through RNA isolation and genetic engineering, these mouse mAbs were humanized or chimerized to reduce immunogenicity in humans[61]. One such humanized mAb, 47D11, demonstrated the ability to neutralize shared epitopes between SARS-CoV and SARS-CoV-2 in Vero cell culture, highlighting its potential as a therapeutic agent against both viruses[64].

Food & Drug Administration Expansion of Authorization of Two mAbs for the Treatment of COVID-19 in Younger Children (including Newborns)

The U.S. FDA has expanded the EUA for bamlanivimab and etesevimab. Previously authorized for pediatric patients aged 12 years and older weighing at least 40 kilograms, the EUA has been extended to include younger pediatric patients, including newborns. This expanded authorization allows for the combined use of bamlanivimab and etesevimab to treat mild-to-moderate COVID-19 in younger pediatric patients who have tested positive for the virus[65]. Additionally, the combination therapy can now be used as a post-exposure prophylaxis to prevent COVID-19 infection in pediatric patients, including newborns, who are at high risk of severe disease or death[66].

COVID-19 Prevention

The COVID-19 pandemic has spurred urgent efforts to develop effective vaccines and therapies. While vaccine development typically takes several years, concerted global efforts have accelerated the timeline for COVID-19 vaccines, with some vaccines becoming available within a year[67]. For individuals who cannot receive vaccination or require immediate protection, monoclonal antibodies (mAbs) offer a promising alternative. By targeting specific viral proteins, mAbs can neutralize the virus and prevent infection or reduce disease severity. Passive administration of mAbs can provide immediate protection, especially for high-risk individuals such as the elderly, immunocompromised, and those with underlying health conditions[68].

However, it's important to note that mAbs are not a long-term solution and should be used judiciously. As vaccine rollout continues, mAbs can play a crucial role in bridging the gap between vaccination and the development of protective

immunity. Additionally, mAbs can be particularly beneficial for individuals who have been exposed to the virus but have not yet developed symptoms[13].

Adverse Effects

One potential side effect of mAb therapy is an allergic reaction. These reactions often occur during or shortly after the infusion and are typically monitored by healthcare providers. Patients who have received anti-SARS-CoV-2 mAbs have experienced a range of hypersensitivity reactions, including anaphylaxis, infusion-related reactions, hives, itching, rashes, diarrhea, dizziness, and pruritis[69]. Additionally, other adverse effects such as fever, chills, nausea, headache, breathing difficulties, hypotension, facial swelling, wheezing, and muscle pain have been reported. Moreover, subcutaneous administration of casirivimab and imdevimab has been associated with injection site reactions, including bruising and redness[70].

EMERGING MONOCLONAL ANTIBODIES

The landscape of mAb therapies for COVID-19 is rapidly evolving. While initial mAbs effectively targeted the original SARS-CoV-2 strain, the emergence of new variants has necessitated the development of next-generation mAbs with enhanced potency and broader spectrum of activity. These novel mAbs are being designed to neutralize multiple SARS-CoV-2 variants, including those with mutations that confer resistance to earlier therapies[71]. Additionally, researchers are exploring mAbs that can modulate the host immune response to COVID-19, potentially reducing disease severity and improving patient outcomes[72].

Next-Generation

The development of mAbs targeting conserved regions of the SARS-CoV-2 virus has emerged as a promising strategy to combat the ongoing pandemic. By focusing on these regions, researchers aim to develop mAbs that are less susceptible to viral mutations and can effectively neutralize a broader range of variants. This approach has the potential to provide long-lasting protection against future outbreaks and variants of concern[73].

Bispecific and Multispecific

A promising avenue in the development of SARS-CoV-2 therapeutics involves the use of innovative antibody-based strategies. Bispecific and multispecific antibodies, which can simultaneously bind to multiple epitopes on the SARS-CoV-2 spike protein, offer a compelling approach to neutralize the virus effectively. By targeting multiple epitopes, these antibodies can reduce the risk of viral escape mutations, which can render conventional monoclonal antibodies ineffective[74].

Long-Acting

Many emerging mAbs are being developed with extended half-lives, offering several advantages. By increasing the duration of their presence in the bloodstream, these mAbs can provide longer-lasting protection against diseases and reduce the frequency of dosing. This is especially beneficial for vulnerable populations, such as the elderly, immunocompromised individuals, and those with chronic conditions, who may require ongoing prophylaxis to prevent infections or disease progression[75].

Enhanced Delivery Mechanisms

To enhance patient convenience and compliance, significant efforts are being directed towards developing innovative delivery mechanisms for mAbs. By formulating mAbs for intramuscular or subcutaneous injection, healthcare providers can administer these therapies outside of hospital settings, reducing the burden on patients and healthcare systems. These advancements have the potential to revolutionize the treatment of various diseases, making mAb therapy more accessible and effective[76].

Combination Therapies

Combination therapy with mAbs and antiviral drugs offers a multifaceted approach to combat viral infections. By targeting different stages of the viral life cycle, such as viral entry, replication, and release, these therapies can disrupt multiple aspects

of viral pathogenesis. This can lead to enhanced antiviral activity and potentially prevent the emergence of drug-resistant viral strains[77].

Broad-Spectrum

Broad-spectrum antibodies offer a promising avenue for combating future coronavirus outbreaks. These antibodies are designed to target conserved regions of the viral spike protein, enabling them to neutralize a wide range of coronaviruses, including SARS-CoV-2. By developing and deploying broad-spectrum antibodies, we can potentially enhance our preparedness for future pandemics and reduce the impact of emerging viral threats[14,78].

Adaptive mAb Platforms

Adaptive mAb platforms represent a promising approach to counter the rapid evolution of viruses like SARS-CoV-2. By utilizing advanced technologies such as phage display and yeast display, these platforms enable the rapid generation of new mAbs with enhanced affinity and specificity for emerging viral variants. This accelerated development process can significantly reduce the time required to develop effective therapeutics and vaccines[79]. Furthermore, adaptive mAb platforms can be tailored to target specific viral epitopes, making them less susceptible to viral escape mutations. As viral pathogens continue to evolve, the development and optimization of adaptive mAb platforms will be crucial for maintaining effective public health strategies[80].

Clinical Trials and Regulatory Pathways

Several mAbs are currently in various stages of clinical trials to evaluate their safety and efficacy against COVID-19. These mAbs target specific viral proteins, neutralizing the virus and preventing infection. Regulatory agencies worldwide are actively working to expedite the approval process for these promising therapies, recognizing the urgent need for effective treatments to combat the ongoing COVID-19 pandemic[14,30].

FUTURE OF MONOCLONAL ANTIBODIES

The potential of mAbs in treating a wide range of diseases is substantial, and ongoing research aims to further optimize their use. While mAbs have proven to be effective therapeutic agents, challenges such as complex manufacturing processes, immunogenicity, and administration routes remain. To address these limitations, researchers are actively exploring innovative strategies to enhance mAb production, improve delivery methods, and reduce adverse immune responses.

A promising strategy involves the development of antibody-drug conjugates (ADCs), which combine the specificity of antibodies with the potency of cytotoxic drugs. ADCs target specific cells, delivering the cytotoxic payload directly to cancer cells while minimizing damage to healthy tissues. This targeted approach offers significant advantages over traditional chemotherapy, which often leads to systemic toxicity. By selectively eliminating cancer cells, ADCs can reduce adverse side effects and improve patient quality of life[81,82].

A recent advancement in mAb therapy involves bispecific antibodies, which possess two distinct antigen-binding sites. This unique characteristic enables them to target multiple antigens simultaneously, often directing cytotoxic T cells to eliminate malignant cells. While these innovative therapies hold immense promise, their clinical application is currently limited to patients who have exhausted standard-of-care treatment options. This limitation arises from rigorous regulatory processes and the need for extensive clinical trials to establish safety and efficacy profiles. Although promising data has emerged from various studies, large-scale, head-to-head comparisons against standard-of-care treatments are still awaited. Nonetheless, the potential of bispecific antibodies to revolutionize cancer therapy is undeniable, potentially rendering more invasive treatments like stem cell transplants obsolete.

CONCLUSION

Monoclonal antibodies have emerged as a promising therapeutic strategy for COVID-19, despite the inherent challenges associated with their development and production. Over the past three decades, mAbs have successfully treated various diseases, demonstrating their efficacy and ease of administration. Their potential application in COVID-19 treatment is

particularly compelling, as they can be derived from recovered patients, providing a rapid and targeted approach. Currently, over 70 mAbs are undergoing clinical trials, promising a swift response to future outbreaks. While vaccines offer long-term protection, mAbs can provide immediate relief and temporary immunity, especially for vulnerable populations like the elderly and immunocompromised individuals. By complementing vaccination strategies, mAbs can offer a comprehensive approach to combatting COVID-19 and future pandemics.

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DATA AVAILABILITY

None.

CONFLICT OF INTEREST

The authors declare no conflicts of interest related to this study.

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