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New Monoclonal Antibodies as Prophylaxis-Therapy for the Last Sars-Cov-2 Variants: A Literature Review and Clinical Experience

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Abstract

Despite the end of the pandemic, COVID-19 continues to pose a serious health threat. Most individuals have established robust immune protection and do not develop severe disease but the infection can still lead to marked and sometimes long-lasting disease symptoms. In the late summer of 2023 a new SARS-CoV-2 variant emerged, BA.2.86 (Pirola), which, based on genetics, differs markedly from all previously circulating variants. As the New Year takes off, CDC continues to track the rise of JN.1 across the World. An offspring of BA.2.86, JN.1 is now the most widely circulating variant of SARS-CoV-2 in the United States and globally. At this time, there is no evidence that JN.1 causes more severe disease. As of December 2024, JN.1 is estimated to account for approximately 62% (range 55-68%) of all currently circulating SARS-CoV-2 variants, an increase from the estimated prevalence of 44% (range 39-50%) two weeks ago. CDC is also observing an increase in the prevalence of JN.1 in international travelers and wastewater viral levels, as well as in most regions around the globe. The challenges of outpatient administration and associated costs, Monoclonal Antibodies were a mainstay of the COVID-19 armamentarium from November 2020, when bamlanivimab first received US Food and Drug Administration emergency use authorization (EUA), through November 2022 [1-3]. Ideal qualities of treatments include effectiveness in preventing hospitalization and death, safety and tolerability for patients, easy administration in the outpatient environment, and cost-effectiveness. Monoclonal antibodies (mAbs) that neutralize SARS-CoV-2 fit the safety and efficacy profile in early randomized clinical trials. This minireview of Clinical Experience explain the importance of Monoclonal Antibodies as Prophylaxis and Therapy areThe Best Opportunity to change the Clinical History in the Sars-Cov-2 Variants Era.

Keywords: Monoclonal Antibodies; Early treatment; Prophylaxis

Introduction

COVID-19, the illness caused by SARS-CoV-2, emerged in late 2019 and spread very quickly across the globe. Within the first two years of the COVID-19 pandemic, more than 774 million cases were reported worldwide. By December 2024, Omicron subvariants, particularly XBB and BQ.1, remain the primary variants of concern, continuing to evolve with significant immune-evasion properties. Though they generally cause milder illness compared to earlier variants like Delta, these subvariants continue to present challenges, especially in the context of reinfections. Early research data from multiple labs are reassuring and show that existing antibodies work against the new variants. These data are also encouraging because of what it may mean for the effectiveness of the 2023-2024 COVID-19 vaccine [4-5]. Monoclonal antibodies targeting the anti-SARS-CoV-2 spike (S) protein are prescribed in high-income countries to prevent severe disease in at-risk patients. Although studies report efficacy as between 50–85% [6], global access is currently largely inequitable. Multivariant omicron (B.1.1.529) and subvariant (BA.2 followed by BA.4 and BA.5) dominance has challenged the treatment landscape for mild-to-moderate disease, introducing considerable certainty on the efficacy of monoclonal antibodies [7-8] and leading to changes to initial recommendations for some

of them. Contemporaneously, oral, direct-acting antivirals with a reported efficacy ranging from 30% (molnupiravir) to 89–90% (nirmatrelvir/ritonavir) have recently received conditional or emergency approval in some countries and been recommended in international guidelines such as the World Health Organization guidelines. S-217622, also known as ensitrelvir, a 3CL protease inhibitor that has been shown to significantly reduce the infectious viral load, is currently in phase 3 trials and waiting for emergency approval in Japan and should be submitted soon in China. The main purpose of this opinion paper is to highlight the possible strategies to optimize and protect current and future therapeutic options to treat the most vulnerable patients.

Emerging Variants of Concern (VOC)

Several variants of concern (VOCs), such as Alpha (B.1.1.7), Beta (B.1.351), Delta (B.1.617.2), Omicron (B.1.1.529), and its subvariants, have shown significant changes in the spike protein, the primary target for many monoclonal antibodies. These variants have displayed varying degrees of resistance to neutralization by monoclonal antibodies that were effective against earlier strains. The Omicron subvariants, in particular, have presented substantial challenges due to their increased transmissibility and the ability to evade immune responses.

Key Variants of Concern (VOCs) in December 2024

Omicron Subvariants (still dominant)

While the Omicron variant (B.1.1.529) originally emerged in late 2021, it continues to dominate globally due to its high transmissibility and ability to evade some immune defenses. As of December 2024, several Omicron subvariants have emerged, each with unique mutations in the spike protein and other regions of the genome. Some of these subvariants have shown increased resistance to immunity induced by previous infections and vaccines [8,9].

The dominant subvariants include

XBB Subline ages

- **XBB.1.5** (also known as "Kraken") remains one of the most prominent Omicron sublineages. It has demonstrated increased transmissibility compared to earlier Omicron variants and some resistance to neutralizing antibodies. However, vaccines and previous immunity still offer protection against severe disease.
- **XBB.2** and **XBB.2.3**: These subvariants are part of the broader XBB lineage, with XBB.2.3 showing increased immune evasion, potentially making reinfections more likely, though severe cases remain relatively rare with timely treatment.

BA.4 and BA.5 Subvariants

- BA.5 still circulates in some regions, albeit at lower frequencies compared to newer Omicron subvariants like XBB. It remains associated with breakthrough infections, especially in individuals who received vaccines targeting older versions of the virus.

BQ.1 and BQ.1.1

- These subvariants were widely discussed earlier in 2024 due to their increased immune evasion properties, making them capable of partially escaping immunity from both vaccination and prior infection. They represent a continued evolution of the Omicron lineage and are a significant concern in terms of reinfection rates.

Potential New Variants to Watch

While Omicron continues to dominate, researchers have been keeping an eye on new variants that may emerge from different branches of the viral tree. As SARS-CoV-2 evolves, the likelihood of new variants that could impact public health increases. Here are some emerging variants and key features:

BA.2.86 (Pirola)

- This variant, also known as Pirola, has gained attention due to its significant mutations in the spike protein, leading to concerns over immune evasion. It's still unclear how it will perform in terms of transmissibility and severity, but some evidence suggests it may evade immunity from both vaccines and prior infections. However, as of December 2024, BA.2.86 hasn't spread as rapidly as other Omicron subvariants.

Centaurus (BA.2.75)

- Although BA.2.75 (Centaurus) was initially identified in mid-2022, newer subvariants within this lineage have continued to evolve. Some studies indicate potential immune evasion, particularly among individuals who have been vaccinated with the original mRNA vaccines.

Other Potential Variants

- Experts are watching for new lineages from both Omicron and pre-Omicron strains, though variants like Alpha, Delta, and Beta have become much less common as Omicron continues to dominate.

Key Features of Omicron Subvariants in December 2024

Several important features of these Omicron subvariants are crucial to understanding their behavior:

- **Immune Evasion**: One of the defining characteristics of recent Omicron subvariants, such as XBB and BQ.1, is their ability to partially evade immunity from both vaccination and prior infections. This means that even if people have been vaccinated or previously infected with SARS-CoV-2, they can still become reinfected.
- **Transmissibility**: Omicron subvariants tend to have high transmissibility compared to earlier variants, including Delta. This increased transmissibility continues to drive outbreaks in some areas, although public health measures and vaccination efforts have helped mitigate the impact.
- **Vaccine Efficacy**: Vaccines based on the original strain of SARS-CoV-2 may offer reduced protection against infection with newer subvariants. However, the vaccines still provide strong protection against severe disease, hospitalization, and death. The availability of updated (bivalent) vaccines that target Omicron lineages has helped improve protection against these subvariants.
- **Severity**: Overall, Omicron subvariants appear to cause less severe disease than earlier variants like Delta, particularly in individuals with immunity from vaccination or prior infection. However, certain groups, such as the elderly, immunocompromised individuals, and those with underlying health conditions, still face a higher risk of severe illness

Recent Scientific Findings on the Immunology of New Variants of Sars-Cov-2: JN.1 and BA.2.86

Because of the sequence divergence of BA.2.86, there was initial concern of a significant reduction in antibody activity. Preliminary data from laboratory-studies from multiple investigators suggest similar antibody activity against BA.2.86 as compared to other currently circulating viruses. CDC and other experts are reassured by these research findings that support the effectiveness of this type of immunity against this variant. Additionally, based on CDC's experience with past SARS-CoV-2 variants, people will likely have protection against severe disease mediated by both cellular and antibody immunity. Real-world data are needed to fully understand the impact given the complexities of the immune response to this variant. Additional studies on this are ongoing, and we expect to learn more in upcoming weeks.

New study sheds light on the biological properties of new COVID variant BA.2.86 (Pirola) and JN.1

The researchers discovered that the Pirola variant, in contrast the all previously circulating Omicron variants, enters lung cells with high efficiency and uses the cellular enzyme TMPRSS2 for entry, thereby exhibiting surprising parallels to variants Alpha, Beta, Gamma and Delta that circulated during the first years of the pandemic. The improved entry into lung cells might indicate that the virus is more aggressive but production of new, infectious viral particles in infected cells was reduced, which may limit spread and pathogenic potential. Finally, the researchers report that the Pirola variant is resistant against all therapeutic antibodies and efficiently evades antibody responses in vaccinated individuals with and without breakthrough infection. However, the virus was appreciably inhibited by antibodies elicited by the new, XBB.1.5-adpated mRNA vaccine. In summary, the results show that four years after the start of the pandemic the virus is still capable of profound changes and can reacquire properties which may promote the development of severe disease [9]. The spread of SARS-CoV-2 is associated with the constant emergence of new viral variants. These variants have acquired mutations in the spike protein, which allow evasion of neutralizing antibodies in vaccinated and convalescent individuals. The emergence of viral variants started with the Alpha variant followed by the Beta, Gamma and Delta variant. At the end of the year 2021 the Omicron variant became globally dominant, which, based on genome sequence, differed markedly from previously circulating variants. However, the virus had to pay a price for this massive change. Thus, the Omicron variant evades neutralizing antibodies and is transmitted with high efficiency but has lost the ability to efficiently use a host cell enzyme, the protease TMPRSS2, for lung cell entry. As a consequence, the Omicron variant induces pneumonia less frequently. CDC and other experts are reassured by these research findings that support the effectiveness of this type of immunity against this variant. Additionally, based on CDC's experience with past SARS-CoV-2 variants, people will likely have protection against severe disease mediated by both cellular and antibody immunity. Real-world data are needed to fully understand the impact given the complexities of the immune response to this variant. Additional studies on this are ongoing, and we expect to learn more in upcoming weeks [10].

BA.2.86 (Pirola) and JN1: A quantum leap in SARS-CoV-2 evolution

Descendants of the Omicron variant dominated globally until the end of the year 2023. New variants frequently differed only by few mutations from their predecessors and there was evidence that viruses circulating in 2023 had only limited options to evade antibody pressure in the human population. Therefore, the discovery of a new SARS-CoV-2 Omicron subvariant, Pirola (BA.2.86), which, based on genome sequence, strongly differed from other circulating viruses drew a lot of attention. The Pirola variant, analogous to the Omicron variant, likely arose in immunocompromised patients and presents a quantum leap in SARS-CoV-2 evolution. The spike protein of the Pirola variant harbors more than 30 mutations relative to its precursor variant,

BA.2, and it is largely unknown how these mutations affect the biological properties of the virus.

BA.2.86 (Pirola) and JN1 can infect lung cells more efficiently

The researchers discovered that the Pirola variant, in contrast to all previously circulating Omicron subvariants, enters lung cells with high efficiency and in a TMPRSS2-dependent manner. Further, they could demonstrate that mutations S50L and K356T in the spike protein of the Pirola variant are important for the highly efficient lung cell entry. "It is noteworthy that two years after the global dominance of the Omicron variant, which fails to robustly enter lung cells, now a quite different virus is spreading and that this virus is able to again enter lung cells with high efficiency. If the augmented lung cell entry translates into more severe disease upon infection with the Pirola variant remains to be investigated in animal models," says Stefan Pöhlmann, head of the Infection Biology Unity of the German Primate Center.

BA.2.86 (Pirola) and JN1 replicates less well than its predecessors

SARS-CoV-2 infected cells produce new virus particles many of which, but not all, are able to infect new cells. The researchers provided evidence that cells infected by the Pirola variant are less well able than cells infected with previous variants to produce intact viral particles. The relatively inefficient production of infectious particles by cells infected with the Pirola variant was surprising. It will be interesting to analyze which mechanism is responsible. Maybe the infected cells produce defective interfering parti.

Signs and symptoms of new variants

The version of the Covid-19 virus behind the latest spike in infections shares many of the same symptoms as earlier variants of Sars-CoV-2: a sore throat, fatigue, headache and a cough. Differences in the symptoms often depend on a person's underlying health and their immune system. But some researchers are reporting among the most common first signs of an infection by JN.1 are diarrhoea or a headache. Fewer patients are losing their sense of smell with variants closely-related to Omicron, of which JN.1 is a subvariant. When Covid first came, it was characterised by these very odd, vague symptoms – from brain fog, feeling exhausted, and losing taste and smell. Now it's mutated to more similar symptoms to the flu, where it's very difficult clinically to distinguish between the two. The virus isn't necessarily less pathogenicRather, it's infecting a population that are less inclined to become sick, because they've seen Sars-CoV-2 before, and they're better at regulating immune response against it. The major lesson over the course of the pandemic is that the symptoms which appear in patients are highly dependent on prior immune status. In the first two years of Covid-19, the responses of an individual patient to the virus were primarily dictated by their state of immune health, along with prior exposure to other coronaviruses. The major lesson over the course of the pandemic is that the symptoms which appear in patients are highly dependent on prior immune status. In the first two years of Covid-19, the responses of an individual patient to the virus were primarily dictated by their state of immune health, along with prior exposure to other coronaviruses. Now, in 2024, this is determined by a much more complex cocktail of factors, including how many times that person has already been infected by the virus, their vaccination status, and whether their vaccination-induced immunity might be on the wane. As a result, the people now experiencing Covid-19 for the very first time are at greater risk, especially if it has been a while since their last booster vaccine. There are still people who have somehow managed to remain completely Covid-näive. If they are unvaccinated or under vaccinated, they stand to have the highest risk of severe and protracted symptoms. Still, Sars-CoV-2 is also constantly mutating, something which is also subtly shifting how it attempts to invade the human body. The JN.1 variant has an elevated ability to evade the immune system, for example, compared to other Omicron sub-variants. But this is also altering the way it affects the human body.

The Systemic Complications of Jn.1

One of the ongoing concerns remains the virus' ability to cause damage to blood vessels and internal organs through the creation of micro clots. In 2023, researchers at Virginia Commonwealth University's School of Medicine reported that people now being infected with Omicron-related subvariants are just 6-7% as likely to lose their sense of smell or taste, compared to infections by the virus in the early stages of the Covid-19 pandemic. Instead, some researchers that patients are more likely to present either with diarrhoea or a headache having been infected with JN.1 or the EG.5 variants. There has been a huge shift in viral tropism, meaning which cells get infected. And that's governed by the sequence of the spike protein. Almost everybody in the world has been infected or vaccinated, so the virus is under huge pressure to escape those immune responses to continue to transmit, so the spike protein has evolved a lot. This leads to it infecting different cells to gain entry, which is why people aren't losing their smell or taste anymore. Researchers are still trying to figure out whether some more subtle, internal consequences of Sars-CoV-2 infection varies between variants of the virus or whether any differences are more driven by the waning of previous vaccine-induced protection. One of the ongoing concerns remains the virus' ability to cause damage to blood vessels and internal organs through the creation of micro clots, with the kidney – an organ which is constructed of approximately one million tiny blood vessels –

seemingly particularly vulnerable based on the patients Strain has seen. We are seeing more microvascular complications and a step change in the kidney function with the new JN.1 variant that does appear to be worse than the past couple of variants. But it's difficult to say whether it's the variant, or the fact its 18 months to two years now since a lot of people last received a vaccine.

Protecting Emerging Treatment Options

Several crucial issues warrant urgent attention to optimize the use of these emerging treatment options (Figure 1). First, as proven to be transformational for HIV, rapid, affordable access to early antiviral treatment to slow the tide of new variants is critical to effective "test-and-treat" strategies to protect the most fragile patients and avoid a severe and/or persistent infection. After more than 2 years of pandemic, progress has been slow [11] and public health attention has recently been attracted by the low-profile agreement during the) in Geneva in May 2022.

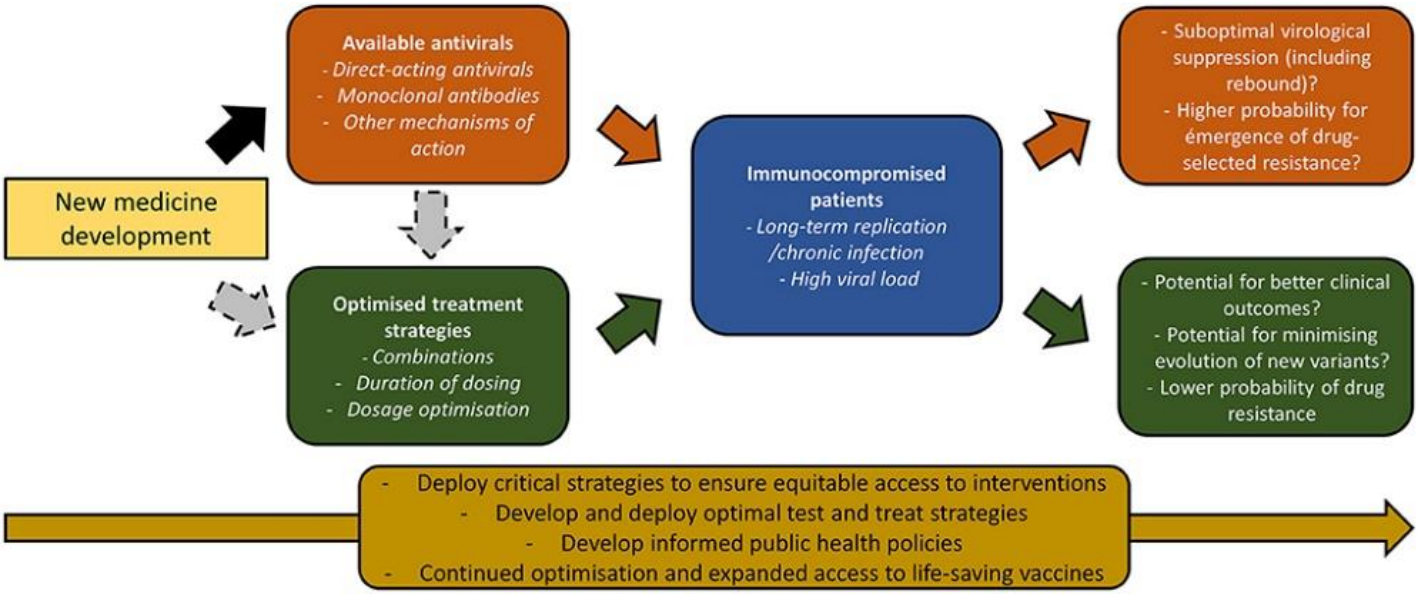

Figure 1: *Potential impact of SARS-CoV-2 antiviral drugs optimization in protecting available antivirals in the shifting landscape of new variants.*

Together with vaccination, early diagnosis and treatment have the ability to reduce disease worsening, to reduce transmission and to constrain variability in viral sequences. Second, although the combined effect of omicron and increasing vaccine deployment in some regions has shifted the demand response from hospital to outpatient care, considerable uncertainty exists about who is now at risk for severe omicron disease [12]. While the risk/benefit ratio across at-risk subpopulations has unquestionably changed in vaccinated populations, gains made can only be preserved if those at highest risk are rapidly diagnosed and receive treatment in less than one week. Third, high levels of antiviral efficacy will be critically important, especially in immunocompromised patients who are grossly underrepresented in registrational trials [13]. Causes of immunosuppression are diverse (including organ/stem cell transplants, cancer, immunosuppressive medications or uncontrolled HIV) and these patients represent a significant proportion of the population, e.g., 7 million adults in the USA [14] , but also in low- and middle-income countries due to the high prevalence of uncontrolled HIV. Overall, the mortality risk with omicron is still unclear, but protection of those who cannot be effectively vaccinated or protected by a prior SARS-CoV-2 infection remains imperative. Importantly, in regions where HIV is highly prevalent, there is a clear need and opportunity to reinforce HIV epidemic control by prompt diagnosis and sustained viral suppression with antiretrovirals, key factors to also enable the control of SARS COV-2 spread in this group. Although there are many other causes for variant emergence (host jump or adaptation, vaccine exposure, to name the most frequent), data confirm that immunocompromised patients with long-term SARS-CoV-2 replication are particularly susceptible to resistance and transmissible variant emergence. The emergence of resistance mutation thus impacting treatment efficacy is more likely if a patient has been exposed to specific antiviral drugs. In addition, it remains unclear if the small percent rebound occurrence (2%) observed with nirmatrelvir/r in the EPIC-HR (Evaluation of Protease Inhibition for COVID-19 in High-Risk Patients) trial, performed in the delta variant era, is underestimating a risk that would be particularly of concern in patients harboring an impaired immune system and in the omicron era. In one recent case series, one out of 7 patients who had a virologic rebound also

had an immunosuppressing condition. Another recent case series revealed that all three patients with viral rebound were highly immunocompromised. This potentially raises concerns about the need of longer antiviral courses, especially in these patients. Preclinical data have clearly demonstrated that virological efficacy is higher for combinations of existing antiviral drugs than single agents. To achieve the goal of changing the treatment guidelines in SARS-CoV-2-infected immunocompromised individuals, independent and academic clinical trials for drug combinations should be considered as an urgent, unmet research priority. Today, collaboration with industry to allow early access to antiviral drugs to be combined has been an objective still to be achieved. Certain potent monoclonal antibodies, such as bebtelovimab, cannot even be accessed for research or for routine care outside of the USA [15-16].

Latest Monoclonal Antibodies and Their Efficacy against New Variants

Recent developments in monoclonal antibody therapies have focused on targeting newer variants of SARS-CoV-2. Here are some of the most promising monoclonal antibodies currently under investigation or authorized for use:

Bebtelovimab

- **Target**: The spike protein, specifically the receptor-binding domain (RBD).
- **Efficacy**: Bebtelovimab has shown activity against several Omicron subvariants, including BA.2 and BA.4/BA.5. However, its efficacy has been reduced against some more recent Omicron sublineages, leading to evolving recommendations for its use.
- **Indication**: It has been authorized for use in patients with mild to moderate COVID-19 who are at high risk of progressing to severe disease, including those who are immunocompromised or elderly.

Evusheld (AstraZeneca's tixagevimab and cilgavimab)

- **Target**: The spike protein.
- **Efficacy**: This combination has been shown to be effective against many variants, including Omicron, and is currently used both for pre-exposure prophylaxis and post-exposure treatment in high-risk individuals. However, recent studies indicate that its efficacy against newer Omicron subvariants (e.g., XBB) may be reduced.
- **Indication**: Recommended for immunocompromised individuals who may not respond well to vaccination or who are at increased risk of exposure.

Casirivimab and Imdevimab (REGEN-COV)

- **Target**: The spike protein, blocking the virus from entering human cells.
- **Efficacy**: This combination has demonstrated variable effectiveness against the Omicron variants, with significant reductions in neutralization against some subvariants. As a result, the FDA withdrew its emergency use authorization (EUA) for this mAb for treatment of COVID-19 in certain regions.
- **Indication**: Previously used for mild to moderate cases in high-risk patients, but less relevant with the emergence of resistant variants.

Sotrovimab

- **Target:** The spike protein.
- **Efficacy:** Sotrovimab was initially effective against several VOCs, but its efficacy against Omicron and its subvariants (particularly BA.4/BA.5) is now limited. The monoclonal antibody is no longer authorized in regions where Omicron subvariants predominate.
- **Indication:** Earlier used for mild to moderate COVID-19 treatment in high-risk patients, but replaced by more effective alternatives in most settings.

Arctivimab and Cilgavimab (Bamlanivimab, Etesevimab)

- **Target:** Spike protein**.**
- **Efficacy:** This combination showed reduced efficacy against Omicron and its subvariants. However, they remain relevant for earlier strains like Delta**.**
- **Indication:** Previously used in high-risk populations, but largely superseded by newer agents due to reduced effectiveness against current VOCs.

Use in Immunocompromised and Elderly Populations

Immunocompromised and elderly patients are at a heightened risk of severe COVID-19 outcomes, and many do not respond adequately to vaccines. Monoclonal antibodies provide an important therapeutic option for these groups, particularly in preventing disease progression and reducing hospitalization rates [17].

Immunocompromised Patients

- Individuals with conditions such as cancer, HIV/AIDS, or those undergoing immunosuppressive treatments (e.g., organ transplant recipients) may not mount an adequate immune response to vaccination. For these patients, monoclonal antibodies can serve as a critical bridge to protection.

- Monoclonal antibody treatments, such as Evusheld, have been used for pre-exposure prophylaxis in these individuals, offering protection against infection and severe disease. However, as new variants emerge, updated monoclonal antibody therapies that can effectively neutralize these strains are critical.

Elderly Patients

- Elderly individuals, particularly those over the age of 65, are at higher risk of severe disease due to age-related decline in immune function and the presence of comorbidities such as diabetes, hypertension, and cardiovascular disease.
- Monoclonal antibodies have shown a role in both treatment and prevention in this group, providing significant benefits when administered early in the course of infection.
- As with immunocompromised patients, it is important that monoclonal antibody treatments are updated to address the evolving viral landscape, particularly in the face of more immune-evasive variants

Challenges and Limitations

- **Resistance to New Variants**: One of the main challenges is the growing resistance of newer variants to existing monoclonal antibodies. As the virus continues to evolve, there is an ongoing need for the development of monoclonal antibodies that can target conserved regions of the spike protein or other viral components.
- **Distribution and Accessibility**: The availability of monoclonal antibodies varies by region, and distribution to high-risk populations, especially in low-resource settings, remains a challenge.
- **Side Effects and Safety**: While monoclonal antibodies generally have a favorable safety profile, some side effects, such as allergic reactions, are possible. Careful monitoring is required, particularly for immunocompromised and elderly patients who may have other health conditions.

Current Public Health Measures

Vaccines and Boosters

- Updated vaccines (e.g., bivalent vaccines) that target both the original strain and Omicron variants are crucial tools in preventing severe illness. These vaccines are being updated periodically to address the evolving variants.

Testing and Surveillance

- Ongoing genomic surveillance is vital to detect emerging variants quickly. Public health authorities closely monitor the emergence of new variants and provide updated guidance based on the virus's behavior.

Treatment and Therapeutics

- Treatments like monoclonal antibodies and antiviral drugs (e.g., Paxlovid) are still used to manage severe cases, particularly in high-risk populations. However, the effectiveness of some monoclonal antibodies has been reduced against certain variants, prompting the development of new treatments.

Public Health Guidelines

Masking, social distancing, and other preventative measures are still recommended in certain settings, especially in areas with high transmission rates or when dealing with vulnerable populations.

Conclusion

The ongoing evolution of SARS-CoV-2 variants necessitates the continuous development of monoclonal antibodies (mAbs) that can neutralize new and emerging strains. For immunocompromised patients, mAbs like Evusheld, Bebtelovimab, and newer combination therapies offer crucial options for prevention and treatment, especially for those at high risk of severe disease. As the virus continues to mutate, ongoing research, including the development of bispecific new monoclonal antibodies and long-acting therapies, will be key to improving outcomes in these vulnerable populations. The future research into new variants and improved vaccines will be critical in preventing future surges and mitigating the impact of SARS-CoV-2 on global health.

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