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Bebtelovimab: The FDA-approved Monoclonal Antibody for Treating Patients with Mild-to-Moderate COVID-19

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Coronavirus disease 2019 (COVID-19) is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). As of February 18, 2022, there were about 420 million confirmed cases of the disease resulting in about 5.86 million deaths worldwide. The first case of this disease was identified in Wuhan, China, in late December 2019. After that, the disease has widely spread throughout the world, causing an ongoing pandemic. COVID-19 symptoms include fever, cough, headache, fatigue, loss of smell or taste, and breathing difficulties. In addition, some infected individuals may lack noticeable symptoms. According to the clinical data, most infected individuals (81%) develop mild to moderate symptoms, whereas 14% develop severe symptoms, and 5% experience critical symptoms. Patients with severe symptoms experience dyspnea, hypoxia, and a great level of lung involvement on computerized tomography scan imaging (more than 50%). However, patients with critical symptoms experience respiratory system failure and multiorgan dysfunction resulting in mortality (1).

COVID-19 vaccines are broadly referred to as the main reason for the reduction in the severity and mortality caused by COVID-19 compared to the pre-vaccine era (4, 5) (2, 3). Many countries have prioritized the vaccination of individuals at the highest risk for COVID-19 complications (such as aged people) and individuals with a higher risk of virus exposure and transmission (such as healthcare workers and professionals). As of February 18, 2022, 10.42 billion COVID-19 vaccines have been administered globally, and about 30 million doses are now administered daily (4). There are various COVID-19 vaccines available in different countries. These vaccine types use different molecular mechanisms for immunization and immunity against SARS-CoV-2. Pfizer-BioNTech, Oxford-AstraZeneca, Sinopharm BIBP, Moderna, and Janssen are examples of COVID-19 vaccines administered in distinct countries.

Although COVID-19 vaccines have controlled the fast spread of SARS-CoV-2, safety concerns rise each time a new virus variant is identified. Biopharmaceutical companies and researchers reevaluate the effectiveness of the administered vaccine doses against the newly discovered variant. Concerning the mentioned vaccines, it is safe to declare that different vaccines may have variable rates of effectiveness against various SARS-CoV-2 variants. However, what is obvious is that vaccination against COVID-19 has decreased the number of patients with severe disease symptoms who need hospitalization. Such patients may require early clinical intervention and an effective line of therapy before further disease spread.

Immunotherapy is one of the candidates for this purpose. Monoclonal antibodies are among the first options with the potential to neutralize the binding component of SARS-CoV-2. On February 11, 2022, the US Food and Drug Administration emergency(FSA) used emergency use authorization (EUA) for a monoclonal antibody, named Bebtelovimab, to treat COVID-19 patients with mild to mod-

erate symptoms leaning towards progression to a severe disease requiring hospitalization (5). To be eligible for this type of therapy, patients must be at least 12 years old and weigh at least 40 kg. Moreover, other FDA-approved COVID-19 treatments must be inaccessible or clinically ineffective for patients to be eligible for bebtelovimab therapy (5).

Bebtelovimab, also known as LY-CoV1404, is a neutralizing human immunoglobulin G1 (IgG1) monoclonal antibody developed by Eli Lilly and AbCellera. This monoclonal antibody was isolated from a patient who had recovered from COVID-19. Bebtelovimab binds the spike (S) proteins of SARS-CoV-2, preventing the virus from binding to ACE2 on the target cell surface and internalization. The S protein is a component of SARS-CoV-2 that causes COVID-19 and is usually used in vaccination mechanisms for immunizing individuals against COVID-19 (6). Pseudovirus and authentic virus assessments have demonstrated that bebtelovimab neutralizes the Omicron variant of SARS-CoV-2. The Omicron variant is currently known as the predominant SARS-CoV-2 variant in the US and many other countries. In addition to the mentioned virus variant, pseudovirus testing has also demonstrated that bebtelovimab has a potent neutralization ability against various other SARS-CoV-2 variants, including BA.2 (6).

Bebtelovimab received FDA approval based on a phase 2 clinical trial (BLAZE-4, NCT04634409). In this trial, non-hospitalized patients who had mild-to-moderate COVID-19 symptoms were administered bebtelovimab (the authorized dose: 175 mg) as monotherapy or together with bamlanivimab (700 mg) and etesevimab (1,400 mg). It is worth mentioning that this clinical trial was conducted before the emergence of the Omicron variant. Therefore, no patient enrolled in this study was infected with this variant of SARS-CoV-2. Most patients enrolled in BLAZE-4 were infected with the Delta or Alpha variants of SARS-CoV-2 (5).

Although vaccine-mediated immunity emerges and develops over time, monoclonal antibody-triggered immunity is a passive type of immunotherapy that occurs immediately. After the administration of monoclonal antibodies, neutralizing antibodies bind viruses preventing target cell internalization and subsequent replication. This effect prevents disease progression in the infected individuals and reduces the rate of mortality. Such approaches are significantly required since it has been shown that COVID-19 vaccines do not mediate complete immunity in the vaccinated population. Moreover, the emergence of a new SARS-CoV-2 variant always raises new concerns regarding the effectiveness of the administered vaccines. Therefore, other types of preventive and treatment tools, including post-infection treatment methods, can be considered a giant step towards a normal life in the ongoing COVID-19 era.

Footnotes

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