AstraZeneca gains first approval for Evusheld as COVID-19 treatment

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AstraZeneca's long-acting antibody combination Evusheld has been approved in Japan for both prevention (pre-exposure prophylaxis) and treatment of symptomatic disease caused by SARS-CoV-2 infection: marking the first global marketing approval of Evusheld as a treatment for COVID-19.

Evusheld (formerly known as AZD7442) combines tixagevimab (AZD8895) and cilgavimab (AZD1061) - derived from B-cells donated by convalescent patients after SARS-CoV-2 infection. The antibody combination was discovered by Vanderbilt University Medical Center and licensed to AstraZeneca in June 2020.

Evusheld gained emergency use authorization in the US for prevention of COVID-19 in December 2021, offering an alternative to vaccination for those who cannot receive a vaccine or do not mount a sufficient immune response (it has also now been authorized for prevention in the EU and a number of other countries).

The Japanese approval, however, marks the first approval for both prevention and treatment. In treatment, trials showed the combination 'significantly reduced' the relative risk of COVID-19 progressing to severe illness or death.

AstraZeneca continues to progress submissions for Evusheld for both prevention and treatment around the world.

Japanese approvals

In prevention, Japan's Ministry of Health, Labour and Welfare (MHLW) granted Evusheld Special Approval for Emergency for adults and adolescents (12 years of age and older weighing at least 40kg). Evusheld is approved for use in those whom SARS-CoV-2 vaccination is not recommended and who may have an inadequate response to a COVID-19 vaccine due to immunodeficiencies.

In treatment, Evusheld is approved for adults and adolescents (12 years of age and older weighing at least 40kg) with risk factors for severe SARS-CoV-2 infection who do not require supplemental oxygen.

Kazuhiro Tateda, M.D. Ph.D., Professor, Department of Microbiology and Infectious Disease, Toho University, Tokyo, Japan, said: *"COVID-19 continues to have a significant impact on our daily lives in Japan. Many people, including older adults, patients with comorbidities, and immunocompromised patients, remain at risk for poor outcomes from severe COVID-19. Evusheld will be a much-needed new option, offering long-term protection for those who do not achieve an adequate immune response after vaccination and helping prevent severe disease and death in those who do become infected."*

The Japanese government has agreed to purchase 300,000 units of Evusheld (150mg each of tixagevimab and cilgavimab), and AstraZeneca is working with the government and partners to make first doses available as soon as possible.

Discovered by Vanderbilt University Medical Center, the human monoclonal antibodies bind to distinct sites on the SARS-CoV-2 spike protein and were optimized by AstraZeneca with half-life extension and reduction of Fc effector function and complement C1q binding.

The half-life extension more than triples the durability of its action compared to conventional antibodies; data from the PROVENT Phase III trial show protection lasting six months.

The reduced Fc effector function aims to minimize the risk of antibody-dependent enhancement of disease - a phenomenon in which virus-specific antibodies promote, rather than inhibit, infection and/or disease.

The approvals were based on efficacy and safety data from the Evusheld clinical development program, including the Provent Phase III pre-exposure prophylaxis trial, the Tackle Phase III outpatient treatment trial, and Phase I trials, including in Japan.

In Provent, a 300mg intramuscular (IM) dose of Evusheld significantly reduced the risk of developing symptomatic COVID-19 by 77% compared to placebo at the primary analysis. An 83% relative risk reduction was shown at a six-month median follow-up analysis, with protection from the virus lasting six months.

In pre-specified analyses of participants who received treatment within three days of symptom onset, Evusheld reduced the risk of developing severe COVID-19 or death (from any cause) by 88% compared to placebo, and the risk reduction was 67% when participants received Evusheld within five days of symptom onset.

The recommended dose for prevention of symptomatic disease caused by SARS-CoV-2 infection in Japan is 150mg of tixagevimab and 150mg of cilgavimab, administered as separate sequential IM injections. Depending on the prevalence of SARS-CoV-2 variants, 300mg of tixagevimab and 300mg of cilgavimab may be administered for prevention. The recommended dose for treatment of COVID-19 is 300mg of tixagevimab and 300mg of cilgavimab, administered as separate sequential IM injections.

Evusheld has been shown to retain in vitro neutralization activity against the main Omicron variants currently circulating globally, including BA.5 and BA.2.

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