AZD7442 prophylaxis trial met primary endpoint

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AZD7442 PROVENT Phase III prophylaxis trial met primary endpoint

in preventing COVID-19

77% reduced risk of developing symptomatic COVID-19

First long-acting antibody combination to prevent COVID-19

Positive high-level results from the PROVENT Phase III pre-exposure prophylaxis trial showed AstraZeneca's AZD7442 achieved a statistically significant reduction in the incidence of symptomatic COVID-19, the trial's primary endpoint.

AZD7442, a combination of two long-acting antibodies (LAAB), reduced the risk of developing symptomatic COVID-19 by 77% (95% confidence interval (CI): 46, 90), compared to placebo. The trial accrued 25 cases of symptomatic COVID-19 at the primary analysis.

There were no cases of severe COVID-19 or COVID-19-related deaths in those treated with AZD7442. In the placebo arm, there were three cases of severe COVID-19, which included two deaths.

AZD7442 is the first antibody combination (non-vaccine) modified to potentially provide long-lasting protection that has demonstrated prevention of COVID-19 in a clinical trial.

The trial included 5,197 participants in a 2:1 randomisation AZD7442 to placebo. The primary analysis was based on 5,172 participants who did not have SARS-CoV-2 infection at baseline.

More than 75% of participants had co-morbidities, which include conditions that have been reported to cause a reduced immune response to vaccination.

The LAAB was well tolerated and preliminary analyses show adverse events were balanced between the placebo and AZD7442 groups.

Myron J. Levin, MD, Professor of Pediatrics and Medicine, University of Colorado School of Medicine, US, and principal investigator on the trial, said: "The PROVENT data show that one dose of AZD7442, delivered in a convenient intramuscular form, can quickly and effectively prevent symptomatic COVID-19. With these exciting results, AZD7442 could be an important tool in our arsenal to help people who may need more than a vaccine to return to their normal lives."

Mene Pangalos, Executive Vice President, BioPharmaceuticals R&D, said: "We need additional approaches for individuals who are not adequately protected by COVID-19 vaccines. We are very encouraged by these efficacy and safety data in high-risk people, showing our long-acting antibody combination has the potential to protect from symptomatic and severe disease, alongside vaccines. We look forward to sharing further data from the AZD7442 Phase III clinical trial programme later this year."

AZD7442 was optimised using AstraZeneca's proprietary YTE half-life extension technology, which could afford up to 12 months of protection from COVID-19, and is delivered by intramuscular injection.

Preliminary 'in vitro' findings from investigators at Oxford University and Columbia University demonstrate that AZD7442 neutralises recent emergent SARS-CoV-2 viral variants, including the Delta variant.[1-6]

AstraZeneca will prepare regulatory submission of the prophylaxis (PROVENT and STORM CHASER) data to health authorities for potential emergency use authorisation or conditional approval of AZD7442. Full results from PROVENT will be submitted for publication in a peer-reviewed medical journal and presented at a forthcoming medical meeting.

PROVENT

PROVENT is a Phase III, randomised, double-blind, placebo-controlled, multi-centre trial assessing the safety and efficacy of a single 300mg dose of AZD7442 compared to placebo for the prevention of COVID-19. The trial was conducted in 87 sites in the US, UK, Spain, France and Belgium. 5,197 participants were randomised in a 2:1 ratio to receive a single intramuscular (IM) dose of either 300mg of AZD7442 (n = 3460) or saline placebo (n = 1,737), administered in two separate, sequential IM injections.

The primary efficacy endpoint was the first case of any SARS-CoV-2 RT-PCR positive symptomatic illness occurring post dose prior to day 183. Subjects will continue to be followed for 15 months.

Participants were adults 18 years-old and over who would benefit from prevention with the LAAB, defined as having increased risk for inadequate response to active immunisation (predicted poor responders to vaccines or intolerant of vaccine) or having increased risk for SARS-CoV-2 infection, including those whose locations or circumstances put them at appreciable risk of exposure to the SARS-CoV-2 virus. Participants at the time of screening were unvaccinated and had a negative point-of-care SARS-CoV-2 serology test.

Approximately 43% of participants were 60 years and over. In addition, more than 75% had baseline co-morbidities and other characteristics that are associated with an increased risk for severe COVID-19 should they become infected, including those with immunosuppressive disease or taking immunosuppressive medications, diabetes, severe obesity or cardiac disease, chronic obstructive pulmonary disease, chronic kidney and chronic liver disease. Approximately 73% were White/Caucasian, 17% Black/African American, and 3% Asian. Approximately 15% of participants were Hispanic.

AZD7442

AZD7442 is a combination of two LAABs - tixagevimab (AZD8895) and cilgavimab (AZD1061) - derived from B-cells donated by convalescent patients after SARS-CoV-2 virus. Discovered by Vanderbilt University Medical Center and licensed to AstraZeneca in June 2020, the human monoclonal antibodies bind to distinct sites on the SARS-CoV-2 spike protein[7] and were optimised by AstraZeneca with half-life extension and reduced Fc receptor and complement C1q binding. The half-life extension more than triples the durability of its action compared to conventional antibodies and could afford up to 12 months of protection from COVID-19 following a single administration.[8-11] The reduced Fc receptor binding aims to minimise the risk of antibody-dependent enhancement of disease - a phenomenon in which virus-specific antibodies promote, rather than inhibit, infection and/or disease.[12]

AZD7442 is being studied in a comprehensive clinical trial programme for both prevention and treatment of COVID-19 in over 9,000 participants. Ongoing trials include TACKLE COVID-19[13], a Phase III treatment trial in an outpatient setting and collaborator treatment trials in outpatient and hospitalised settings. AZD7442 is being assessed in both IM and intravenous administration routes.

AZD7442 is being developed with support from the US Government, including federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response; Biomedical Advanced Research and Development Authority in partnership with the Department of Defense; Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense, under Contract No. W911QY-21-9-0001.

AstraZeneca is working with governments around the world to make AZD7442 accessible to high-risk populations as another valuable option in the fight to end COVID-19, should it prove to be effective and well tolerated.

Data published in *Nature* in July 2020 showed that in preclinical experiments, the LAABs were able to block the binding of the SARS-CoV-2 virus to host cells and protect against infection in cell and animal models of disease.[14]

Under the terms of the licensing agreement with Vanderbilt, AstraZeneca will pay single-digit royalties on future net sales.

AstraZeneca

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Contacts

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