Phase 3 trial reports one dose of Ad5-nCoV COVID-19 vaccine is safe and effective, including against severe disease

December 24 2021

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One dose of Ad5-nCoV (Convidecia), a COVID-19 vaccine developed in China, is 57.5% effective against symptomatic COVID-19 and 91.7%

effective against severe COVID-19 disease beginning 28 days postvaccination, according to a phase 3 randomised controlled trial published in *The Lancet*.

The report indicates that Ad5-nCoV is safe, with no serious vaccine-related adverse events or deaths reported among trial participants, and that the vaccine induces a robust antibody response.

Developed by CanSino Biologics, Inc. and the Beijing Institute of Biotechnology, Ad5-nCoV is single-dose viral vector vaccine that can be stored between 2°C and 8°C. The vaccine has been approved for emergency use in 10 countries, including Argentina, Chile, Mexico, and Pakistan, where this current clinical trial took place. Regulatory review is in progress in Russia, which also participated in this clinical trial.

"Our study suggests that one dose of Ad5-nCoV is highly effective against severe disease— potentially helping to ease the tremendous strain COVID-19 has put on health systems around the world by keeping people from becoming seriously ill or requiring hospitalisation. In addition, because the vaccine is effective against severe disease after one injection, it could help provide improved access to vaccination, especially in low- and middle-income countries, where it can be more challenging to reach people with a two-dose primary vaccination course," says study lead author Dr. Scott Halperin, Dalhousie University, Canada.

The trial, which is still ongoing, commenced on September 22, 2020, and, by January 15, 2021, had enrolled 36,982 adults 18 years of age and older, of which 36,727 were randomized to receive either a vaccine or placebo injection across 66 enrolment sites at study centers in Argentina, Chile, Mexico, Pakistan, and Russia.

The researchers conducted an efficacy analysis once the protocol

threshold of 150 laboratory-confirmed (RT-PCR positive) symptomatic COVID-19 at 28 days post-injection was reached on January 15, 2021, at which point there were 21,250 trial participants in the primary efficacy cohort. Researchers reported 105 positive COVID-19 cases out of 10,590 participants in the placebo group and 45 positive COVID-19 cases out of 10,660 participants in the vaccine group, resulting in an efficacy of 57.5% at 28 days postvaccination.

Efficacy against severe disease was 91.7% at 28 days post-vaccination, where severe disease was defined as a minimum of one of clinical signs at rest indicative of severe systemic illness, respiratory failure, evidence of shock, significant acute renal, hepatic, or neurologic dysfunction, or admission to an ICU. There were no COVID-19-related deaths among vaccine recipients.

As reported in phase 1 and 2 trials [3] Ad5-nCoV was well tolerated and produced high levels of anti-RBD antibodies and neutralizing antibodies.

The majority of the adverse events, including pain at the injection site, headache drowsiness, and generalized muscle aches were mild to moderate and occurred within seven days of injection. There were no reports of thrombosis or thrombocytopenia in any study participants.

The authors caution that the efficacy analysis was conducted in samples collected on or before January 15, 2021, and therefore don't include analysis on more recent variants of concern such as the delta and omicron variants.

"More research is needed to determine Ad5-nCoV's effectiveness and durability over a longer period of time as well as its effectiveness against variants of concern, including omicron, which is rapidly overtaking delta as the dominant strain worldwide," says Dr. Joanne Langley, Dalhousie University, Canada.

The authors note that additional secondary outcomes will also be analysed, including efficacy against asymptomatic infection and efficacy against PCR-negative, seroconversion-positive cases.

Additional ongoing research is underway to explore the relative efficacy of a single- versus two-dose regimen of Ad5-nCoV.

The authors note some further study limitations. Although the study was conducted across five countries, the majority of study participants included in this analysis were from Pakistan (16,950 participants) and Mexico (13,559 participants); this was mainly due to the trial being first initiated at sites in Pakistan on September 22, 2020 followed by Mexico on November 6, 2020. People with unstable medical conditions, people who were pregnant, and children were excluded from the study. Women and older individuals were also under-represented. Although researchers employed active case finding methods through weekly contact via phone calls and text messages, signs and symptoms were self-reported (although confirmed through in-person study visits) and therefore not all positive cases may have been included. Further research is underway to determine Ad5-nCoV's long term durability and effectiveness against variants of concerns.

Writing in a linked Comment, Dr. Richard Kennedy of the Mayo Clinic, USA, who was not involved in the study, says, "Despite remarkable accomplishments in SARS-CoV-2 vaccine development and production, there are still large regions of the world where access to vaccines remains limited. In some areas of the world vaccine hesitancy is also an obstacle to achieving high vaccination coverage. In addition to these challenges, there is waning immunity from the SARS-CoV-2 vaccines and a continued emergence of variants capable of different degrees of immune evasion. Thus, there is a clear and urgent need for the continued development, testing, and use of additional vaccines…The study provides important data supporting the continued use of another

adenovirus vectored vaccine. The continued monitoring of this study population will be necessary to answer ongoing questions related to waning immunity, the duration of protection, the need for booster vaccination, and the ability to protect against new variants, including omicron."

More information: Scott A Halperin et al, Final efficacy analysis, interim safety analysis, and immunogenicity of a single dose of recombinant novel coronavirus vaccine (adenovirus type 5 vector) in adults 18 years and older: an international, multicentre, randomised, double-blinded, placebo-controlled phase 3 trial, *The Lancet* (2021). DOI: 10.1016/S0140-6736(21)02753-7