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Efficacy of an adenovirus type 5 vectored SARS-CoV-2 vaccine

Published Online
 December 23, 2021
[https://doi.org/10.1016/S0140-6736\(21\)02834-8](https://doi.org/10.1016/S0140-6736(21)02834-8)
 See [Article](#) page 237

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.¹ In some areas of the world vaccine hesitancy is also an obstacle to achieving high vaccination coverage.² 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.

In *The Lancet*, Scott Halperin and colleagues³ report the results of a double-blind, randomised, placebo-controlled, endpoint-case driven, phase 3, clinical trial of a single dose of an adenovirus type 5 vectored vaccine (CanSino Biologics, Tianjin, China) in adults 18 years and older. The study involved 18 363 vaccinated and 18 354 unvaccinated participants from Argentina, Chile, Mexico, Pakistan, and Russia, with recruitment beginning in September, 2020, and continuing until the endpoint of 150 COVID-19 cases was reached in January, 2021. The racially diverse study cohort was approximately 70% male, and approximately 20% of the participants were aged 45–59 years and approximately 8% were 60 years or older. The primary endpoints were efficacy and safety, with efficacy being measured by the prevention of symptomatic, PCR-confirmed SARS-CoV-2 infection 1 month after vaccination and safety measured by the incidence of

severe adverse events. Vaccine efficacy in preventing symptomatic disease 14 days after vaccination and in preventing severe COVID-19 served as secondary efficacy endpoints.

28 days after vaccination, Efficacy against PCR-confirmed COVID-19 was 57.5% (95% CI 39.7–70.0; $p=0.0026$) and 91.7% (95% CI 36.1–98.9) against severe COVID-19. Similar efficacy numbers have been reported in clinical trials of the Oxford AstraZeneca chimpanzee adenovirus vectored vaccine (62.1% in recipients of the standard dose)⁴ and the Jansen, Johnson & Johnson adenovirus type 26 vectored vaccine (66.9% against COVID-19 and 76.7% against severe COVID-19).⁵ In terms of safety, the authors reported the expected range of systemic and local reactions (fever, headache, and muscle aches, as well as redness, swelling, and pain at the injection site). Serious adverse events were relatively rare, and the rates did not differ between vaccine and placebo groups. Given differences in the timing, geographical region, study cohorts, and circulating variants, these three vaccines appear to have broadly similar safety and efficacy profiles.

Most previous phase 3 clinical trials of COVID-19 vaccines have found that there is a lag period of roughly 14 days between vaccination and the start of protection. Halperin and colleagues report a similar lag period of approximately 12 days.³ Although the reported efficacy was slightly higher at 14 days (63.7% [95% CI 52.9 to 72.1]) than at 28 days post-vaccination, the CIs overlap and no formal analysis comparing the efficacy rates was done. It is also noteworthy that efficacy was substantially lower (17.5% [95% CI –127.6 to 70.1]) in participants aged 60 years and older than participants younger than 60 years, suggesting that additional vaccine doses might be necessary in this age group.

The study has multiple strengths including the large cohort size of over 18 000 vaccine recipients; the global nature of the study, with recruitment sites in multiple countries allowing for greater racial and ethnic diversity; the inclusion of older adults (aged >60 years); the clear definitions of COVID-19 and severe COVID-19; and weekly contact with participants to actively identify cases and retain a high participant



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retention. These strengths increase the reliability of the findings.

However, this study also presents some limitations. One of these is the short follow-up time (<2 months for most people) available at this preplanned analysis point. The short follow-up means that the current report cannot provide additional information to address current concerns about the longevity of vaccine-induced protection; however, as the trial continues, this information should become available. Additional limitations are that women represented only approximately one third of the total cohort (and approximately 29% of the primary efficacy cohort) and that the majority of the participants were from Mexico (36.9%) and Pakistan (46.2%). These study characteristics might limit the generalisability of the results. The authors did perform subanalyses to explore these issues: efficacy is reported by sex, with lower efficacy in women than men at both timepoints, and efficacy is reported by country and body-mass index. The authors do indicate that these and other important follow-up analyses will be part of the long-term monitoring of the trial cohort. As with most clinical trials, individuals with compromised immune systems, unstable medical conditions, and other potential risk were excluded and we will need to wait until real-world effectiveness studies are done to ascertain the ability of the vaccine to provide protection in these vulnerable groups.

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.⁶

I report being the inventor of and holding a patent for SARS-CoV-2 PolyPeptides and receiving royalties paid by Initiatives to Change the World (ICW) Healthcare Ventures for this patent and other intellectual property covering the development of peptide-based vaccines.

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Late thrombectomy for ischaemic stroke

Patients with ischaemic stroke tend to delay seeking professional help compared with patients with acute myocardial infarction with ST elevation (STEMI). Moreover, for patients with STEMI, a diagnosis of ongoing ischaemia can be made with an electrocardiogram in the ambulance. The situation is vastly different for a patient who has had a stroke. Those with cortical infarcts—the case for most patients—are often not aware of their acute deficit, or they cannot communicate because of language problems. Moreover, patients with cerebral ischaemia do not have pain, as patients with STEMI do. They also typically do not wake up when a stroke occurs during sleep. Notification of the stroke to emergency

services often depends on the alertness of partners and bystanders, and it should not be surprising that patients have delays in presenting to the emergency room, typically 3–4 h later than patients with a STEMI.^{1,2} In patients arriving after more than 6 h from onset, diagnosis of ongoing ischaemia caused by intracranial large vessel occlusion has to be made with CT angiography and perfusion imaging, which further adds to the delay.

Initially, guidelines advised endovascular treatment only for patients with ischaemic stroke due to intracranial large vessel occlusion, based on trials in patients who could be treated within 6 h. The treatment effect in these trials diminished with time



Published Online
November 11, 2021
[https://doi.org/10.1016/S0140-6736\(21\)02097-3](https://doi.org/10.1016/S0140-6736(21)02097-3)
See **Articles** page 249