Sputnik V COVID-19 vaccine candidate appears safe and effective

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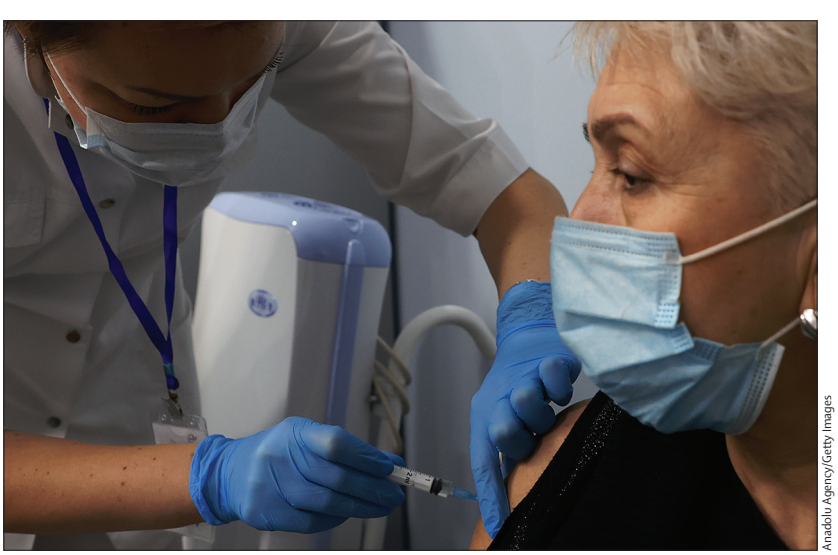
Denis Logunov and colleagues[1] report their interim results from a phase 3 trial of the Sputnik V COVID-19 vaccine in *The Lancet*. The trial results show a consistent strong protective effect across all participant age groups. Also known as Gam-COVID-Vac, the vaccine uses a heterologous recombinant adenovirus approach using adenovirus 26 (Ad26) and adenovirus 5 (Ad5) as vectors for the expression of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein. The use of two varying serotypes, which are given 21 days apart, is intended to overcome any pre-existing adenovirus immunity in the population.[2] Among the major COVID vaccines in development to date, only Gam-COVID-Vac uses this approach; others, such as the Oxford–AstraZeneca vaccine, use the same material for both doses. The earlier vaccine for Ebola virus disease, also developed at Gamaleya National Research Centre for Epidemiology and Microbiology (Moscow, Russia), was similar, with Ad5 and vesicular stomatitis virus as the carrier viruses,[3] and the general principle of prime boost with two different vectors has been widely used experimentally.[4]

The recombinant adenovirus route to protection is shared with the Oxford–AstraZeneca vaccine, which uses a chimpanzee adenovirus (ChAdOx),[5] the Johnson & Johnson vaccine that uses only Ad26[6] whose detailed results are expected soon, and the CanSinoBIO-Beijing Institute of Biotechnology Ad5-based vaccine whose phase 3 trial began in September, 2020.[7] The carrier viruses are modified and cannot initiate a productive infection; they enter cells, express the spike protein, and then stop (because they cannot continue the normal virus lifecycle), although a high-sensitivity analysis also showed that a few Ad genes were expressed, albeit at a low level.[8] The vaccine-infected cells are eventually destroyed by the very immunity they are designed to elicit. Recombinant adenoviruses have been used widely as vaccine vectors because they can accommodate large genetic payloads and, although unable to replicate, they trigger the innate immunity sensors sufficiently to ensure robust immune system engagement.[9] Consequently, they do not need an adjuvant and can provide immunity after just a single dose.[4] Their physical robustness is thought to allow storage at temperatures around –18°C, which is feasible for many supply chains. The downside of recombinant adenovirus-based vaccines is that large doses are required, typically 10^{10} or 10^{11} particles, which makes large demands on the manufacturing and quantitation required for rollout on a global scale.

What then of the Sputnik V COVID-19 vaccine data published here? The earlier phase 1/2 data published in September, 2020, showed promising safety results and gave an indication that the immune response was at a level consistent with protection.[10] Recipients generated robust antibody responses to the spike protein, which included neutralising antibodies, the proportion of the total immunoglobulin that inhibits the virus binding to its receptor. They also showed evidence of T-cell responses, consistent with an immune response that should not quickly wane. The interim report of the phase 3 data now presented[1] includes results for more than 20 000 participants, 75% of whom were assigned to receive the vaccine, and the follow-up for adverse events and infection. With a planned study power of 85%, those recruited were aged 18 years and older, were about 60% male, and were almost all white. Comorbidities, a known risk for COVID-19 severity, were present in about a quarter of those who entered the trial. 62 (1·3%) of 4902 individuals in the placebo



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group and 16 (0·1%) of 14 964 participants in the vaccine group had confirmed SARS-CoV-2 infection from day 21 after first vaccine dose (the primary outcome). A time-resolved plot of the incidence rate in the two groups showed that the immunity required to prevent disease arose within 18 days of the first dose. That protection applied to all age groups, including those older than 60 years, and the anecdotal case histories of those vaccinated but infected suggest that the severity of disease decreases as immunity develops. Three fatalities occurred in the vaccine group in individuals with extensive comorbidities, and were deemed unrelated to the vaccine. No serious adverse events considered related to the vaccine were recorded, but serious adverse events unrelated to the vaccine were reported in 45 participants from the vaccine group and 23 participants from the placebo group. Vaccine efficacy, based on the numbers of confirmed COVID-19 cases from 21 days after the first dose of vaccine, is reported as 91·6% (95% CI 85·6–95·2), and the suggested lessening of disease severity after one dose is particularly encouraging for current dose-sparing strategies.

The development of the Sputnik V vaccine has been criticised for unseemly haste, corner cutting, and an absence of transparency.[11] But the outcome reported here is clear and the scientific principle of vaccination is demonstrated, which means another vaccine can now join the fight to reduce the incidence of COVID-19.

We declare no competing interests.

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