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Covid-19: Russia approves vaccine without large scale testing or published results

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The Russian government has approved a covid-19 vaccine for widespread use despite it apparently undergoing only a phase I trial (38 people) with no published results.

The announcement was made on national television when the president, Vladimir Putin, said, "I know that it works quite effectively, forms strong immunity, and I repeat, it has passed all the needed checks."[1]

He claimed that one of his daughters had been given the vaccine. Members of the Russian elite have reportedly also received doses of the vaccine since April.[2]

The chief of the Russian Direct Investment Fund, Kirill Dmitriev, has said that a phase III trial will start in August and will involve thousands of people in Russia, Saudi Arabia, and the United Arab Emirates. The vaccine could then be distributed as early as September.

The approval of a vaccine without large scale testing has caused concern, and researchers have called for the results to be published for scrutiny and for further trials to take place before the vaccine is rolled out to the public.

"Russia has granted a licence based on phase I data: this would not be done anywhere else in the world," said Robin Shattock, who is leading a team working on an RNA vaccine candidate for covid-19 at Imperial College London. "If the Russian data is as good as reported in press briefings, then the data will speak for itself when released."

Trials

More than 165 SARS-CoV-2 vaccine candidates are currently being assessed around the world, of which eight are undergoing phase III trials and two have been approved for limited use—the Russian vaccine and a Chinese vaccine.[3] The Chinese government has specially approved the drug company CanSino's Ad5-nCoV vaccine to be used in the armed forces.[4]

The Russian vaccine has been developed by the Gamaleya Institute, Moscow, and uses two human adenovirus vectors and the SARS-CoV-2 spike protein to produce an immune response. The institute previously caused controversy amid reports that it tested its vaccine on soldiers and that researchers dosed themselves during shortened human trials. Meanwhile, Canada, the UK, and the US have accused Russia of trying to steal vaccine research, although Russian officials have denied this.

The clinical trials database states that two almost identical trials have been registered by the Gamaleya Institute, both involving 38 people. One trial involves Gam-COVID-Vac Lyo[5]—a "lyophilisate for the preparation of a solution for intramuscular administration"—and the other uses Gam-COVID-Vac,[6] a covid-19 vaccine candidate given by intramuscular injection.

The Gam-COVID-Vac trial reported that nine participants were given a recombinant adenovirus vector based on the human adenovirus type 26 containing the SARS-CoV-2 S protein gene, and another nine were given the same but using a human adenovirus type 5 vector. A separate group of 20 were given both, the first on day 1 and the second on day 21.

The record said that patients would be followed up during four visits—carried out seven, 14, 28, and 42 days after administration of the drug and again at 90 and 180 days. However, it also stated that the study would begin on 17 June 2020 and end on 10 August 2020, which would not allow for the 180 day follow-up (about six months).

The primary endpoints of the study were the "changing of antibody levels against the SARS-CoV-2 glycoprotein S in 42 days" and the number of participants with adverse events. The secondary measures were "changing of virus neutralizing antibody titer" and "changing of antigen-specific cellular immunity level."

Safety and efficacy

Shattock told *The BMJ*, "Licensing a vaccine requires demonstration of safety and efficacy in thousands of participants. The signs are that the Russians will perform such testing, although it is unclear if trials will be of significant size.

"If the vaccine is shown to be effective then that would be significant; however, such studies will take many months to complete. It would be worrying if any vaccine was rolled out before such rigorous testing—but that doesn't appear to be the case at this stage.

"Russia has a strong track record in vaccine development. I suspect they would not want to undermine their reputation by shortcutting established pathways of development."

Meanwhile, Ayfer Ali, a specialist in drug research at Warwick Business School, has warned that, without proper testing, researchers could miss potential antibody dependent enhancement (ADE)—"a phenomenon where a vaccine is not protective enough to prevent the disease but instead allows the virus to enter the body more easily and worsen the disease the vaccine is supposed to protect against."

She warned, "This has been observed in animal models of non-covid-19 coronavirus vaccines before. When such a phenomenon is observed in small studies testing can be stopped and the damage limited. When this happens at the population level, it can have devastating effects. That is one reason proper testing is paramount. Russia is essentially conducting a large, population level experiment."

The vaccine is being referred to as "Sputnik V," a reference to the first satellite launched into orbit around the Earth during the cold war space race between the US and the USSR.

Ohid Yaqub, senior lecturer in the science policy research unit at the University of Sussex, said, "I would hope that other countries are not drawn into such 'pork barrel' vaccine nationalism . . . The less that vaccine development looks like this, the better.

"Decision making should be published, open to scrutiny, and free from flag waving. We should resist allowing vaccine development to be used as a measure of national scientific prowess."

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3 Corum J, Grady D, Wee SL, Zimmer C. Coronavirus vaccine tracker. *New York Times* 2020 Aug 12 (updated). https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html.

4 Mahase E. Covid-19: Where are we on immunity and vaccines? *BMJ* 2020;370:m3096. doi: 10.1136/bmj.m3096 pmid: 32759299

5 An open study of the safety, tolerability and immunogenicity of "Gam-COVID-Vac Lyo" vaccine against covid-19. *ClinicalTrials.gov* 2020 Aug 12 (updated). https://clinicaltrials.gov/ct2/show/NCT04437875?term=vaccine&cond=covid-19&draw=4.

6 An open study of the safety, tolerability and immunogenicity of the drug "Gam-COVID-Vac" vaccine against covid-19. *ClinicalTrials.gov* 2020 Aug 12 (updated). https://clinicaltrials.gov/ct2/show/NCT04436471?term=vaccine&cond=covid-19&draw=4.