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The arrival of Sputnik V

Controversy continues to brew around Russia's newly minted COVID-19 vaccine, Sputnik V. Vijay Shankar Balakrishnan reports.

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For more on **the phase I trial of Sputnik V** see **Articles**
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On Aug 11, Russia announced the launch of Sputnik V, its home brewed adenovirus-based vaccine candidate against COVID-19 and by Sept 4, the results of its phase 1/2 studies were published in *The Lancet*. However, *The Lancet* paper does not settle the debates around the politics and the science of Sputnik V even though the developers claim it to be the "best vaccine" against COVID-19.

The name Sputnik is explained by Kirill Dmitriev, CEO of the state-run sovereign wealth fund, Russian Direct Investment Fund (RDIF). "We understood that there would be lots of scepticism and resistance to the Russian vaccine for competitive reasons; therefore, there was a decision to call it a Russian recognisable international name", Dmitriev told *The Lancet Infectious Diseases*.

The Moscow-based Gamaleya Research Institute of Epidemiology and Microbiology then took charge of the Sputnik V's development and clinical trials counting on their experience in studying the platform for Ebola and Middle East respiratory syndrome vaccines. Denis Logunov, *The Lancet* paper's lead author led the yet unpublished animal studies of Sputnik V's safety in rhesus macaque monkeys, rabbits, guinea pigs, rats, and mice, and its efficacy in marmoset monkeys and Gamaleya's own immune-suppressed Syrian golden hamsters, observing a 100% protection from a high degree of infection. However, the design of the first human trial of Sputnik V drew criticisms.

Sheena Cruickshank, an immunologist at University of Manchester, UK, thinks that the results of this open-labelled, non-randomised study overestimate treatment effects with Sputnik V, because the association between intervention and outcome could be influenced by a third factor, such as the influence of a doctor.

Despite not being made aware of the quality control or quality assurance details of the Sputnik V, vaccinologist Peter Hotez (Baylor College of Medicine, Texas, USA) sees notable merits in the Russian vaccine: the freeze dried formulation of Sputnik V—much similar to the smallpox vaccine developed by the Soviet Union in the 1970s—allows the vaccine to be transported to distant locations circumventing a cold chain; the tolerability is similar to the other adenovirus vectored vaccines; and the overall levels of virus neutralizing antibodies are not high even with the two doses, but similar to some of the other adenovirus vectored vaccines. "Although it's difficult to compare virus neutralising antibodies between studies, in non-human primates with the AstraZeneca Oxford vaccine, they achieved similar levels but only partial protection upon virus challenge", Hotez told *The Lancet Infectious Diseases*. However, Cruickshank thinks the variable and insignificant levels of neutralising antibodies are concerning. "The levels of these indicators shown are highly variable, so it's difficult to draw firm conclusions as to whether the vaccines were eliciting a robust T cell response", Cruickshank said.

To vaccinologist Tracy Hussell (University of Manchester, UK), although Gamaleya used a well-trodden path of priming the immune response with one adenovirus carrying the spike protein of severe acute respiratory syndrome coronavirus 2 and then boosting it with a different adenovirus carrying the same protein, it is possible that the immune response secondary to a previous exposure to adenovirus, which is a common cause of colds, might affect the vaccine.

Against this backdrop, the phase 3 trials of Sputnik V have already begun. However, the required 40 000 volunteers stirred a political and human rights debate. Some Russian media reports cite the Federation contemplating to roll out a mass vaccination programme for Sputnik V. The head of a trade union for physicians, Anastasia Vasilieva (The Doctors' Alliance, Moscow), who exposed the flaws in Russia's COVID-19 numbers, questions the plans for mass vaccination and mandating volunteering as a "real sabotage".

Ideally, Russia should loop in the World Health Organization and other bodies with interest in COVID-19 vaccine development such as the Coalition for Epidemic Preparedness Innovations and Gavi, The Vaccine Alliance. However, at the time of writing, WHO's spokesperson Tarik Jasarevic said to *The Lancet Infectious Diseases*, "Any safe and effective pandemic vaccine will be a global public good, and WHO urges rapid, fair, and equitable access to any such vaccines worldwide", adding, "WHO is in touch with Russian scientists and authorities and looks forward to reviewing details of the trials".

To Thomas Cunei (International Federation of Pharmaceutical Manufacturers & Associations, Geneva), no matter how urgently action is needed against the COVID-19 public health emergency, it is imperative for the vaccine makers to upheld the highest standards of quality, safety, and efficacy. "Lack of transparency on results of preclinical or clinical trials, let alone transparency on due process remains concerning."

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