Self-amplifying RNA COVID-19 vaccine technology safe in humans, suggests study

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Dr Katrina Pollock. Credit: Imperial College London

Results from the first trial of a new COVID-19 vaccine technology show no short-term safety concerns.

The data, from scientists at Imperial College London, suggests the technology can generate immune responses against COVID-19 in up to 87 percent of people, even at extremely low dose levels—the lowest of any COVID-19 vaccine candidate worldwide.

The technology uses genetic code called self-amplifying RNA (saRNA). This genetic information holds instructions to make a protein found on the outside of the coronavirus, called the spike protein.

Once injected into the muscle of the arm, the cells make this spike protein, enabling the immune system to generate defenses against the virus.

The team, who published their data on a pre-print server, are now refining the technology to produce future vaccines and boosters against COVID-19, and emerging variants.

The team are modifying the technology to produce a more consistent and strong response, even at very low dose levels, and will pursue trials with updated vaccine candidates.

COVID-19 boosters

Professor Robin Shattock, who leads Imperial's COVID-19 vaccine project, said: "Global demand for COVID-19 vaccines will remain high in the coming decade, given the emergence of lethal SARS-CoV-2 escape-variants, and expected requirement for booster vaccination. We have shown the saRNA technology is safe and can generate an immune response. We are now refining the Imperial saRNA platform to develop vaccines for a variety of other infectious diseases."

The ultra-low dose saRNA technology has potential to protect against a variety of other infectious diseases, such as rabies and Ebola. The

researchers also believe it could be developed to treat other conditions, such as cancer.

Professor Shattock said: "The approach is emerging as one of the great scientific advances of the pandemic, with the ultra-low dose offering three key advantages. The first is the potential to manufacture a huge amount—one liter of reaction material can produce up to one million doses.

"The second advantage of a lower dose is the reduced likelihood of side effects. Finally, a low dose vaccine opens up the possibility of combining the COVID-19 vaccine with other vaccines. We may now need annual vaccines against COVID-19, and a lower dose makes combination with other vaccines, such as the flu vaccine, more feasible."

New trials begin as vaccine candidate updated

In the trial, 192 participants aged 18-45 years received a variety of doses of the saRNA vaccine, at either four or 14 weeks apart. The results showed participants produced mixed responses. Some achieved good levels of neutralizing antibodies, while others had very limited immune responses.

The doses ranged from 0.1 micrograms to 10 micrograms of saRNA , with 87 percent of people generating antibodies to SARS-CoV-2, the virus that causes COVID-19. For comparison, the Moderna and Pfizer mRNA vaccines have dosages of 100 and 30 micrograms, respectively.

Side effects experienced by the participants were low, with the most common being chills and muscle ache, and there were no allergic reactions.

The research team, who have submitted their trial data to a peer-

reviewed journal, are now working on modifying the technology to produce a more consistent and strong response, even at very low dose levels. They have recently started a new trial with an updated vaccine candidate designed to increase responses by enhancing the level of RNA expression.

More information: Katrina M. Pollock et al, Safety and Immunogenicity of a Self-Amplifying RNA Vaccine Against COVID-19: COVAC1, a Phase I, Dose-Ranging Trial, *SSRN Electronic Journal* (2021). DOI: 10.2139/ssrn.3859294

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