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Vaccine by Arcturus and Duke-NUS in phase 2 trials

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Three different Covid-19 messenger RNA vaccines, which may have reduced side effects when administered, are being developed with Singapore's involvement in their clinical trials.

Developed by United States firm Arcturus Therapeutics, the three vaccine candidates can be given at a much lower dose than the mRNA vaccines now available – such as those by Pfizer and Moderna – because of the "self-amplifying" mRNA technology they use.

Each dose of the Arcturus vaccine contains 5 micrograms of vaccine, compared with 30mcg in the Pfizer vaccine and 100mcg in the Moderna vaccine.

The first vaccine, known as ARCT-021, targets the wildtype, or original Sars-CoV-2 virus, and was developed together with Singapore's Duke-NUS. Local phase two trials, administered by SingHealth's Investigational Medicine Unit, are ongoing.

The two newer vaccines – ARCT-154 and ARCT-165 – target the four variants of concern, Alpha, Beta, Gamma and Delta.

The local clinical trials will evaluate the vaccines' safety and immune response against the variants, and as possible booster shots for people who have received the Pfizer vaccines, said Associate Professor Jenny Low, the unit's deputy clinical and scientific director.

Arcturus chief executive Joseph Payne told The Straits Times that while both vaccines have shown effectiveness against the variants when tested on primates, the ARCT-154 showed a stronger response to the Delta variant, while the ARCT-165 had a bias for the Beta variant.

The ARCT-154 vaccine is also undergoing clinical trials in Vietnam, in parallel with the trials conducted here. In Singapore, the trials will also evaluate the vaccine as a booster jab. The data for both trials will be pooled together in November, he added.

While conventional mRNA vaccines "teach" the cells to produce the Sars-CoV-2 viral spike protein to trigger an immune response in the body, the self-amplifying mRNA vaccine produces the protein at a lower level for a longer period of time – usually a couple of weeks, said Mr Payne.

The longer duration will generate the same neutralising antibody response in the body as well as help it develop a more robust T-cell response. T-cells are thought to confer long-lasting immunity to the virus and its variants.

In addition, having a lower dose also means that each dose carries fewer lipid nanoparticles that deliver the mRNA and an ingredient known as polyethylene glycol (PEG), which could sometimes trigger a rare allergic reaction known as anaphylaxis. This could potentially improve the vaccine's safety profile, he added.

Asked if the lower vaccine dose would mean a lower chance or incidence rate of myocarditis (heart inflammation), Mr Payne said this was a possibility. But while myocarditis has not been seen in trials for Arcturus' vaccines so far, more robust data is needed, he said.

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While mRNA vaccines "teach" the cells to produce the Sars-CoV-2 viral spike protein to trigger an immune response, the self-amplifying mRNA vaccine produces the protein at a lower level for a longer period of time, says Arcturus Therapeutics chief executive Joseph Payne. PHOTO: ARCTURUS THERAPEUTICS

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