

A vertical, high-magnification electron micrograph of MERS-CoV virus particles. The particles are spherical, with a distinct outer envelope and a darker, textured core. They are scattered across a blue, granular background, with a higher concentration in the upper left quadrant.

KAIMRC a strong player in quest for a MERS-CoV vaccine

The medical hub's research into a single-dose vaccine for the lethal Middle East respiratory syndrome coronavirus (MERS-CoV) is promising, but more evaluation and trials are needed, scientists say.

The search for a vaccine that would curb the threat of Middle East respiratory syndrome (MERS) and stop the virus in its tracks has been central to KAIMRC's clinical research efforts. Now, a new vaccine developed by the centre and tested successfully in camels carries a lot of promise. The new vaccine, ChAdOX1, is now being tested in humans, marking the first phase I clinical trial to be conducted in Saudi Arabia.

The kingdom was the site of the first MERS-Coronavirus (MERS-CoV) infection and has reportedly experienced the worst outbreaks of the virus. MERS-CoV-related fatalities have reached 851 globally, with 773 in Saudi Arabia alone, according to figures released by the World Health Organisation (WHO) this September. So far, MERS-CoV infections have reached a total of 2,468 worldwide, including 2077 infections in Saudi Arabia.

MERS-CoV, a viral disease caused by a novel



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coronavirus, was first identified in a pneumonic patient in Saudi Arabia in 2012. Patient zero died shortly after contracting the virus, whose symptoms ranged from fever, cough and shortness of breath to diarrhoea and other gastrointestinal symptoms. MERS-CoV is endemic in dromedary camels — possibly the virus's only intermediate animal host, although scientists believe that bats may be putative reservoirs.

Saudi Arabia's research into MERS risk factors, transmission techniques and potential treatments had been at the forefront over the past few years. KAIMRC intensified its own research drive after experiencing a hospital outbreak in 2015, forming collaborations nationally and internationally, including with Oxford University. The hospital "epidemic led KAIMRC to prioritize MERS-CoV and make it one of its

strategic projects," said Ahmed Alaskar, KAIMRC's executive director.

"The MERS-CoV crisis has led to a drastic strategy to promote research and development to reduce the health and economic burdens of this emerging pathogen," added Majed Alghoribi, Chairman of KAIMRC's infectious diseases research department. "And the best way to prevent and tackle the dissemination of the MERS-CoV is to develop camel and human vaccines."

Enter ChAdOX1

As of now, there are no proven antiviral or vaccines to treat or prevent MERS, and none of the vaccines proposed, have yet been licensed for use against the virus. According to Abdelali Haoudi, head of strategy and business development at KAIMRC, there are about 40 potential vaccine candidates worldwide, four of

which were developed in Saudi Arabia.

Among the strongest contenders was an MVA-based vaccine that has been tested in infected camels and which requires two doses to reduce the viral load and provide partial protection. A joint study by KAIMRC's associate research scientist and virologist, Naif Alharbi, Oxford University and the Ministry of Agriculture now proposes a single-dose vaccination, based on a chimpanzee adenoviral viral vector known as ChAdOX1.

Successful vaccination of camels would reduce viral circulation in this host and thereby reduce human exposure," said the study authors. "In addition, developing a vaccine for humans and vaccinating humans at risk, such as camel keepers and healthcare workers, would further control the number of human infections."

The ChAdOX1-based vaccine has been initially tested in mice, with encouraging results, then later in seropositive dromedary camels.

The new vaccine has provoked a strong immune response and proved to be both effective and safe, according to a study in *Scientific Reports*¹. It has also successfully reduced virus replication in camels, according to Alharbi, who describes the outcome of the research as “remarkable.” The vaccine can also potentially protect both camels and humans – a huge turning point for virologists and scientists desperately trying to develop effective anti-MERS vaccination.

Alharbi’s team’s study is reportedly the first of its kind to evaluate a MERS vaccine in dromedaries in endemic countries. “It is also the first to utilise naturally infected camels to assess vaccine efficacy,” said Alharbi.

According to the scientists involved, it has covered considerable ground in only three years, a brief time considering that research into infectious diseases can take decades to yield results.

The first phase I clinical trial in the kingdom

In collaboration with Oxford University scientists, Alharbi is currently working on a human phase I clinical trial for the single-dose vaccine, which is a first in Saudi Arabia. A phase I trial has already launched in Oxford, and is set to start in the kingdom imminently. The structure is set in place, and the Saudi Food and Drug Authority (SFDA) has already given the green light, according to Alaskar, and they are now in the recruiting phase. This will be the first-in-human vaccine to be developed in Saudi Arabia or in an endemic country, according to Alharbi and peers.

“We are expecting to see results in 2020,” said Alharbi.

According to Alharbi, the scientists will also conduct another small study to optimise the vaccine dose and the way it’s administered. “There is still a chance to optimize the single dose to achieve even stronger immune responses in camels.”

Alaskar and Alharbi both said that

“There’s no regulatory pathway to approving a vaccine for camels, not internationally and not in this country, so we’re going for a push for regulation to control vaccines in animals.”

KAIMRC plans to expand the vaccine trials to include a greater number of camels, and they are now working on developing the best protocol for that. “We also need to wait longer to see how long the immunity lasts in these camels,” Alaskar added.

There are challenges, however. Alharbi said that aside from the logistical challenge of sampling 40 camels per day and finding the optimum way for vaccine delivery, the mechanisms of transmission of MERS-CoV among hosts, and its tipping point, are largely mysterious, leaving the scientists in the dark about risks and modes of infection.

Application and pushing the vaccine to the market, following successful trials, could also prove problematic, according to the scientist, making it difficult to start much-needed vaccination.

“It’s not easy to conduct these studies and so we have to be very clever in designing the next experiment,” said Alharbi. “There’s no regulatory pathway to approving a vaccine for camels, not internationally and not in this country,

so we’re going for a push for regulation to control vaccines in animals.”

Alharbi explained that while MERS can be transmitted to anyone around the world, which can potentially cause outbreaks, the endemic areas are limited to a few countries, which is not typically a strong market incentive for vaccine research and development. Promising research could build a stronger case, however, for biopharma to get on board.

KAIMRC’s Mohammad Bosaeed, the clinical trial’s phase I principal investigator, shared his concern that endemic countries still need to prepare for worst-case scenarios. “When you have an outbreak, you need to have a vaccine that is ready to use,” he said.

Alharbi is hopeful, however, that the country will see at least one or two vaccines passing phase II clinical trials in the next five years.

Finally, once a vaccine is approved for veterinary use, explained Alharbi, public health authorities in endemic countries would need to convince camel farmers to immunize their animals, which, despite being hosts of the disease, are not harmed by it.

1. Alharbi, N.K., Qasim, I., Almasoud, A. et al. Humoral Immunogenicity and Efficacy of a Single Dose of ChAdOx1 MERS Vaccine Candidate in Dromedary Camels. *Sci Rep* **9**, 16292 (2019) DOI:10.1038/s41598-019-52730-4

2. Alharbi, N. K., Padron-Regalado, E., Thompson, C. P., Kupke, A., Wells, D., Sloan, M. A. et al. ChAdOx1 and MVA based vaccine candidates against MERS-CoV elicit neutralising antibodies and cellular immune responses in mice. *Vaccine* **35**(30):3780-3788(2017)DOI: 10.1016/j.vaccine.2017.05.032

3. Modjarrad, K., Roberts C.C., et al. Safety and immunogenicity of an anti-Middle East respiratory syndrome coronavirus DNA vaccine: a phase 1, open-label, single-arm, dose-escalation trial. *The Lancet Infectious Diseases* **19** (9): 1013-1022 (2019) DOI: [https://doi.org/10.1016/S1473-3099\(19\)30266-X](https://doi.org/10.1016/S1473-3099(19)30266-X)