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HEALTH

U.K. Tests Efficacy of Mixing Vaccines

Researchers are beginning trials to study the effects of following an initial dose with a booster produced by another manufacturer.

By Jason Douglas

LONDON—As the world keeps adding to its armory of effective vaccines against Covid-19, scientists are starting to ask a new question: What happens if you mix and match?

Researchers are beginning human trials in which volunteers will receive an initial dose of one vaccine and a booster shot from another made by a different manufacturer. The goal is to see if such a strategy—known as heterologous prime-boost vaccination—could produce a more effective immune response against the virus that causes Covid-19 than using two shots of a single vaccine.

Finding ways to bolster the body's defenses has gained new urgency following the emergence of variants of the virus, whose vulnerability to existing shots isn't fully understood.

Researchers said the mix-and-match approach, if validated in human trials, will offer another benefit as countries race to inoculate their citizens: It might help ease pressure on vaccine supplies by giving doctors more options when patients are due for a second dose.

"Knowing that you could mix different vaccine types according to supply availability could only accelerate vaccination efforts," said Helen Fletcher, professor of immunology at the London School of Hygiene and Tropical Medicine.

Researchers at the University of Oxford are enrolling volunteers in an 820-person trial in the U.K. to evaluate a one-two combination of the shot developed by Pfizer Inc. and Germany's BioNTech SE and the vaccine developed by the University of Oxford and AstraZeneca PLC. The trial, partly funded by the U.K. government, was announced by the U.K. Department of Health and Social Care on Thursday.

AstraZeneca said in December that it plans to test its vaccine with Sputnik V, the vaccine developed in Russia, in a human trial. That trial is expected to start soon in Azerbaijan, the United Arab Emirates and other countries.

Immunologists said the mix-and-match strategy is a tried and tested method of enhancing the body's immune response to beat back invaders. Heterologous prime-boost vaccination has been turned against other infectious diseases, including ebola, malaria and tuberculosis, and has been used to sharpen the body's assault against pathogens that cause some cancers and against the tumors themselves.

"I don't see any downside to heterologous prime-boost," said Brian Lichty, associate professor of pathology and molecular medicine at McMaster University in Hamilton, Ontario.

By combining shots that can train the immune system to recognize and attack a pathogen in subtly different ways, the body might assemble a bigger or better-equipped army to beat back any invaders it encounters, according to researchers. The combination strategy might avoid the risk with a traditional two-shot vaccine that the immune system repels the vaccine the second time around.

Russia's Sputnik V follows the mix-and-match idea by using a different viral carrier to train the immune system against Covid-19 in each of its two doses.

The U.K. trial will be the first to test against Covid-19 a mix-and-match approach using different technologies. Pfizer and BioNTech's vaccine relies on molecular couriers known

as messenger RNA to ferry instructions to cells. AstraZeneca's uses a modified chimpanzee virus as a vector to deliver its payload.

"We don't have clinical data for such an approach," said Ugur Sahin, the chief executive of BioNTech. "Therefore, it is important to evaluate the combination of different vaccines within controlled clinical trials before simply implementing this in practice."

Pfizer said in a statement that it recommends using its vaccine in the manner supported by existing trial data but added that decisions on alternative dosing programs reside with health authorities. AstraZeneca said it is supportive of the trials.

Immunologists said mixes of technologies aren't unusual. Scientists at the University of Oxford in January reported in a study awaiting review that combining a different RNA-based vaccine and a viral-vector vaccine generated a strong immune response in mice. Messenger RNA vaccines have been tested in conjunction with viral-vector vaccines in types of cancer.

The goal of the U.K. trial is to test whether a mix-and-match approach works as well as or better than the typical practice, said Matthew Snape, associate professor of pediatrics and vaccinology at Oxford and the trial's leader.

Some participants will get an AstraZeneca shot first and the Pfizer shot second. Others will get the reverse. Control groups will be given the normal two-shot schedule of a single vaccine. The trial will also look at spacing the shots over both four and 12 weeks. Preliminary results are expected in late May or early June, and participants will be monitored closely for side effects. The plan is to enroll more volunteers and test new combinations as additional vaccines gain regulatory approval in the U.K., Prof. Snape said.

Researchers will regularly test participants' blood for antibodies, infection-fighting T-cells and other markers of immune-system activity. They will compare those on the mixed schedule with those on the regular dosing regime to detect any differences. Prof. Snape said researchers will be able to use those samples to gauge the potential effectiveness of a mix-and-match vaccination against coronavirus variants that might not be as vulnerable to standard shots.

Mary Ramsay, head of immunization at Public Health England, a U.K. health agency, said success in the trial could help physicians facing bottlenecks in vaccine supply. A mix-and-match strategy could help if, for instance, someone couldn't get a second dose of the original shot or experienced a bad reaction to the first one.

“It really makes the implementation much more simple,” she said.

Mene Pangalos, AstraZeneca’s executive vice president for biopharmaceuticals research and development, said Wednesday at a press briefing: “Ultimately, we want to understand how interchangeable these vaccines are. These are important questions, because ultimately, people will be using different vaccines at different times.”

Jenny Strasburg and Bojan Pancevski contributed to this article.

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