UNIVERSITY of MARYLAND BALTIMORE

UMB News

Trial Confirms Safety of 'Mix-and-Match' Vaccine Boosters

January 27, 2022 | *By January Payne*

A University of Maryland School of Medicine (UMSOM) Center for Vaccine Development and Global Health (CVD) expert is co-leading an ongoing study that was pivotal in recommending adults and teens receive booster COVID-19 shots of their choosing starting in fall 2021. The preliminary clinical trial results, reported today in *The New England Journal of Medicine*, found that it is safe and effective to receive boosters that are the same or a different one from the person's primary vaccine(s).

Kirsten E. Lyke, MD, professor of medicine at UMSOM, is co-chair and site principal investigator for the study and presented data to the U.S. Food and Drug Administration's (FDA) expert vaccine panel in October that led to the recommendation for mix-and-match booster doses following completion of Emergency Use Authorization (EUA) regimens.

Kirsten E. Lyke, MD, Professor of Medicine at UMSOM, is Co-Chair and site Principal Investigator for the study and presented data to the U.S. Food and Drug Administration's (FDA) expert vaccine panel in October that led to the recommendation for mix-and-match booster doses following completion of Emergency Use Authorization (EUA) regimens.

"This study was pivotal in contributing knowledge about the safety and immune responses of mixing and matching primary vaccines and boosters," said Lyke, who is also the director of CVD's Malaria Vaccine and Challenge Unit. "Boosters are critical against emerging variants of concern, such as the Delta and Omicron variants. The boosters provide an important tool to prevent severe disease, hospitalization, and death."

Meagan Deming, MD, PhD, instructor of medicine at UMSOM, is vice-chair of the study, which is a collaboration between investigators at UMSOM's CVD and the Institute of Human Virology (IHV). IHV investigators **Jennifer Husson, MD, MPH, Joel Chua, MD**, and **Angie Price, DNP, MSN, CRNP**, worked with CVD faculty on this study. The UMSOM Vaccine Treatment and Evaluation Unit (VTEU) is part of the Infectious Diseases Clinical Research Consortium (IDCRC) that investigated the mix-and-match boosters.

The newly published study found that for adults who previously received a full regimen of any COVID-19 vaccine granted EUA or approved by the FDA, an additional booster dose of any of these vaccines was safe and prompted an immune response. The ability to use vaccines for boosting that are different from those used for the primary series — mix and matching — can simplify vaccine booster administration.

These findings are from an ongoing Phase 1/2 trial conducted under UMSOM's VTEU as part of the IDCRC and sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health.

The *NEJM* report describes findings from 458 adult volunteers who had been fully vaccinated with one of the three EUA COVID-19 vaccines at least 12 weeks prior to enrollment. Of those volunteers, 150 study participants received a booster of Johnson & Johnson's Ad26.CoV2-S vaccine; 154 received a booster of Moderna's mRNA-1273 vaccine (100 microgram dose); and 154 received a booster of Pfizer-BioNTech's BNT162b2.

The IDCRC trial, which began enrollment in May 2021, is led by co-chairs Robert L. Atmar, MD, of Baylor College of Medicine, Houston, Texas, and Lyke at UMSOM.

"Mix-and-match is not a new approach. It is a well-known principle in vaccine science research. Mixing vaccine platforms can elicit a stronger, longer-lasting response than a single vaccine regimen and could help us fight variants," said Lyke.

At 15 days after booster vaccination, serum antibody levels increased in all study groups, and leveled off by day 29. For a given primary EUA COVID-19 vaccine, administering a different vaccine as a booster elicited similar or higher serologic responses as compared to their respective homologous booster response. Additionally, T cell responses were measured. Cellular CD4 Th1 T cell responses directed against the spike protein increased in all groups except volunteers who received a single dose of Johnson & Johnson followed by a booster of Johnson & Johnson. However, CD8 T cell responses were more durable in Johnson & Johnson recipients and those who received an mRNA primary series followed by a Johnson & Johnson boost.

Booster vaccines may enhance waning immunity and expand the breadth of immunity against SARS-CoV-2 variants of concern. Heterologous prime-boost strategies may offer immunological advantages to optimize the breadth and longevity of protection achieved with currently available vaccines. They may also simplify the logistics of administering booster vaccines.

"Three COVID-19 vaccines have reached approval or EUA in the U.S. The vaccines made by Moderna and Pfizer-BioNTech are based on messenger RNA, while the Johnson & Johnson vaccine uses viral vectors. The ability to receive initial vaccinations using one approach, followed by a booster that uses the other approach, offers an expanded range of possibilities," said **Karen Kotloff, MD,** professor of pediatrics, associate director for clinical research in CVD, and principal investigator of the UMSOM VTEU. "For example, when supplies are short, or people have side effects to one type of vaccine, having this flexibility can be very important. This study provides reassurance that mixing and matching vaccines is a feasible approach that is well-tolerated and triggers strong immune responses."

The trial participants kept diaries of any side effects and supplied blood samples on the day of booster vaccination and 15 days after boost. More than half of participants reported mild/moderate headache, pain at the injection site, muscle aches, and malaise, which was similar to the primary series. There were no vaccine-related serious adverse events reported.

Study participants will be followed for a year to assess longer-term immune responses. Additional COVID-19 vaccine candidates will be studied in the future.

"We are fortunate to have some of the top vaccine scientists in the world in our Center for Vaccine Development and Global Health — such as Dr. Lyke — leading the way in COVID-19 vaccine research throughout the pandemic," said **E. Albert Reece, MD, PhD, MBA**, executive vice president for medical affairs, University of Maryland, Baltimore, and the John Z. and Akiko K. Bowers Distinguished Professor and dean at UMSOM. "As we confront another variant of COVID-19 — this one the most contagious of all — the availability of the mix-and-match booster approach came just in time for successive waves of the Delta and Omicron variants and likely contributed to saving many lives."

NIAID grants supporting this research are UM1AI48372, UM1AI148373, UM1AI148450, UM1AI148452, UM1AI148573, UM1AI148574, UM1AI148575, UM1AI148576, UM1AI148684, UM1 AI148689 and with support from the NIAID Collaborative Influenza Vaccine Innovation Centers (CIVICs) contract 75N93019C00050.

SHARE THIS ARTICLE