

Mix-and-Match Trial Finds Additional Dose of COVID-19 Vaccine Safe, Immunogenic

An NIH-sponsored study assessed boosters for adults fully vaccinated with any authorized or approved COVID-19 vaccine.

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In adults who had previously received a full regimen of any of three COVID-19 vaccines granted Emergency Use Authorization (EUA) or approved by the U.S. Food and Drug Administration, an additional booster dose of any of these vaccines was safe and prompted an immune response, according to preliminary clinical trial results reported in *The New England Journal of Medicine*.

The findings served as the basis for recommendations by the FDA and the Centers for Disease Control and Prevention in late fall 2021 to [permit mix-and-match COVID-19 booster vaccinations](#) in the United States. Additional data from the ongoing Phase 1/2 trial, sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, are expected in the coming months.

The new report describes findings from 458 adults who had been fully vaccinated with any of three EUA COVID-19 vaccines at least 12 weeks prior to enrollment and who had no reported history of SARS-CoV-2 infection. At enrollment, a single booster dose was administered to each participant: 150 received Janssen/Johnson & Johnson's Ad26.COV2.S vaccine; 154 received Moderna's mRNA-1273 vaccine; and 154 received Pfizer-BioNTech's BNT162b2 vaccine. Depending on which primary vaccine regimen a participant had received, the booster vaccine was either different than (mixed, or heterologous) than or the same as (matched, or homologous) the original vaccine.

The trial participants kept diaries of any side effects. More than half of participants reported headache, pain at the injection site, muscle aches and malaise. No serious vaccine-related adverse events were reported.

All combinations of primary and booster vaccine resulted in increased neutralizing antibody levels (ranging from 4.2- to 76-fold higher levels than those detected prior to boost.) Likewise, all primary-boost combinations increased binding antibody levels 4.6- to 56-fold. For each primary EUA COVID-19 vaccine, heterologous boosts elicited similar or higher antibody responses as compared to responses to a homologous booster. Cellular responses (CD4 and CD8 T cell) also

increased in all but the homologous Ad26.CoV2.S-boosted group, though CD8+ T cells were highest at baseline in those participants who had received the Ad26.CoV2.S EUA vaccine.

Taken together, the investigators concluded, these data strongly suggest that homologous and heterologous booster vaccine will increase protective efficacy against symptomatic SARS-CoV-2 infection.

These interim results cover available immunogenicity data through the initial 29 days following booster vaccination. Investigators will continue to follow participants for one year to assess what impact booster vaccination has on longer-term immune responses. Additional arms of the trial may test other investigational, EUA or FDA-approved COVID-19 vaccines and/or vaccines based on SARS-CoV-2 variants as the boosting vaccine.

The [trial began](#) in May 2021 and is continuing to enroll participants. Its principal investigators are Robert L. Atmar, MD, of Baylor College of Medicine, Houston; and Kirsten E. Lyke, MD, of the University of Maryland School of Medicine, Baltimore. It is being conducted through NIAID's [Infectious Diseases Clinical Research Consortium](#), a clinical trials network that encompasses the Institute's longstanding Vaccine and Treatment Evaluation Units (VTEUs).

Additional information about the trial, including a listing of trial sites enrolling volunteers, is available at [ClinicalTrials.gov](#) using the identifier [NCT04889209](#).

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