Novavax COVID-19 vaccine as a second dose generates high immune response in young people, finds study

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Researchers running the University of Oxford-led Com-COV3 study have reported the results of a study assessing the immune response and side effect profile of "mixed" two-dose COVID-19 vaccine schedules in adolescents aged 12 to 16 years—administering either a full or a one-

third (fractional) dose of the Pfizer-BioNTech COVID-19 vaccine or a full dose of the Novavax vaccine at least eight weeks after a first full dose of the Pfizer-BioNTech vaccine.

In a paper published in the *Journal of Infection*, the researchers report that a mixed schedule using a full dose of Pfizer-BioNTech followed by a full dose of Novavax led to fewer break-through infections and generated higher antibody and T cell responses than the licensed two full dose (homologous) Pfizer-BioNTech schedule against both wild-type COVID-19 and omicron COVID-19 variants, BA.1 and BA.2.

A full dose of Pfizer-BioNTech followed by a fractional (one-third) dose of the same vaccine elicited the lowest antibody concentrations to wild-type COVID-19 but generated similar neutralizing antibodies to two-full-doses of Pfizer-BioNTech against both BA.1 and BA.2.

Although all mixed and non-mixed vaccine schedules used in the study demonstrated favorable side effect profiles, participants who received fractional dose Pfizer-BioNTech as their second vaccine also reported fewer and milder side effects compared to the other study groups. No vaccine-related safety concerns were raised in this study of 148 participants aged 12 to 16.

This research is the first to report the results of a randomized controlled trial examining the immune response and side effect profiles of standard and mixed vaccine COVID-19 vaccine schedules in adolescents. The Com-COV program has now been expanded to include a new study, running across 12 UK National Health Service and academic institutions and backed through funding from the former Vaccine Taskforce (now the COVID Vaccine Unit in the UK Health Security Agency) and the Coalition for Epidemic Preparedness Innovations. This new study will characterize immune responses to third doses of different COVID-19 vaccines following two full doses of Pfizer BioNTech in 12- to 16-year-

olds.

Dr. Angela Minassian, Chief Investigator on the trial from the Oxford Vaccine Group, said, "This study has embodied an incredible effort from our collaborating UK sites and the willing young people who took part. Together we have shown that mixed and fractional doses of COVID-19 vaccine schedules studied are well-tolerated and generate robust immune responses in adolescents for at least eight months.

"Of particular interest is the enhanced performance of Novavax's protein subunit vaccine following a dose of Pfizer-BioNTech's mRNA, compared to the standard two doses of Pfizer-BioNTech mRNA. Among participants who had not been infected with COVID-19 before, those in the Novavax group were less likely to report a breakthrough infection than those in the standard Pfizer-BioNTech group. While interpretation should be cautious considering the study's small sample size, this suggests that a combination of vaccine platforms may result in a greater breadth of protection."

Researchers reported other key findings from the study:

- Reactions were mostly mild-to-moderate, with fewest reactions in the fractional Pfizer-BioNTech group
- Participants in the fractional Pfizer-BioNTech group were more likely to have a breakthrough infection than the standard Pfizer-BioNTech and Novavax groups Antibody responses were similar for all three groups at 236 days after second doses were administered

Dr. Eimear Kelly, Pediatric Research Fellow at the Oxford Vaccine Group, Department of Pediatrics and co-author, said, "The impressive performance of Novavax in this study against wild-type and omicron SARS-CoV-2 variant strains provides supportive evidence for its use as

part of a mixed COVID-19 vaccine schedule. This is important as mixed COVID-19 vaccine schedules allow greater flexibility and improve COVID-19 vaccine supplies globally. We are very grateful to the participants who made this important study possible."

The study was designed as a participant-masked, randomized, and multi-site immunogenicity trial and funded by the Vaccine Taskforce and National Institute for Health and Care research (NIHR).

The current mRNA vaccines recommended by the Joint Committee on Vaccination and Immunization are bivalent vaccines that have been upgraded to target two circulating variants of COVID-19. This study used wild-type mRNA vaccines that targeted the original strain of COVID-19 and therefore cannot be directly compared to the vaccines used in more recent campaigns.

More information: Eimear Kelly et al, Reactogenicity, immunogenicity and breakthrough infections following heterologous or fractional second dose COVID-19 vaccination in adolescents (Com-COV3): A randomised controlled trial, *Journal of Infection* (2023). DOI: 10.1016/j.jinf.2023.06.007

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