Review of: "Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) following two doses of ChAdOx1 nCov-19 or BNT162b2 in the UK (COV-BOOST): a blinded, multicentre, randomised, controlled, phase 2 trial"

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This paper describes the findings of the COV-BOOST study, which administered third dose booster vaccinations against COVID-19. Patients who completed a primary series of ChAdOx1 nCov-19 (Oxford-AstraZeneca) or BNT162b2 (Pfizer-BioNTech) were randomised within 3 groups at 18 sites. Group A had NVX-CoV2373 (Novavax), half dose NVX, ChAdOx1 or meningococcal conjugate vaccine control (MenACWY), Group B had BNT162b2, VLA2001 (Valneva), half dose VLA, Ad26.COV2.S (Janssen) or MenACWY control, while Group C had mRNA1273 (Moderna), CVnCoV (CureVac), half dose BNT162b2 or MenACWY control.

While this paper is useful in that it allows comparisons of vaccine immunogenicity and reactogenicity from a third dose based on a primary series of ChAdOx1 or BNT162b2, there are several limitations in applying these findings in clinical practice due to several reasons. Firstly, the ideal situation of offering patients a range of options for their booster dose based on this paper is unlikely, given the limited vaccine availability at each location. Not all countries used ChAdOx1 or BNT162b2 in the primary series, particularly in developing countries, where vaccines such as Sinopharm, Sinovac and Covaxin were administered in large numbers. In addition, when concerns were raised regarding cerebral venous thrombosis and thrombocytopenia with ChAdOx1, several countries temporarily suspended its use, resulting in heterologous vaccinations with a switch to mRNA vaccines for the second dose.[1] Finally, the FDA authorisation for mRNA vaccine booster doses is as follows: the dose for BNT162b2 is the same as the primary series, while for mRNA1273, half the dose (50mcg) of the primary series is administered.[2] However, the COV-BOOST study groups used half a dose of BNT162b2 and a full dose of mRNA1273 instead.

Another important consideration in interpreting vaccine efficacy is the COVID-19 variant. Currently, Omicron is the predominant variant globally; its multiple mutations confers potential escape mechanisms from vaccine induced immune responses. For example, a Qatar study found only modest effectiveness of booster mRNA doses compared to previous strains, suggesting a need to develop new generations of vaccines, based on the main circulating SARS-CoV-2 variants. [3] While the reactogenicity data from the different vaccine booster combinations in the COV-BOOST study remain useful, the immunogenicity of these combinations will need further evaluation for the Omicron variant.

Finally, while the antibody response from vaccines appear to be the main aspect of interest, its level wanes over time and varies depending on the variant of concern. However, T-cell immunity appears robust over time and preserved against the Omicron variant, despite limited or absent neutralising antibodies.[4] Future studies are required to evaluate post-vaccination T-cell responses and how to optimally induce protective cell-mediated immunity.

References

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