# Safety and Immunological Response following Heterologous Primary Series of COVID-19 Vaccination: The preliminary report focusing on the delta variant

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**Rationale:** The COVID-19 vaccines in Thailand National Program included inactivated vaccines, manufactured by Sinovac (CoronaVac) and adenovirus-vector vaccine by AstraZeneca (ChAdOx1). The emergence of delta variant that escapes the immunity following post-infection or post-vaccination, resulted in reduced the vaccine efficacy. Heterologous prime-boost using the various available vaccines may improve the immunogenicity and provide solution to the limited vaccine supply.

**Objectives:** To assess safety and immunogenicity of heterologous prime-boost using CoronaVac and ChAdOx1 vaccines.

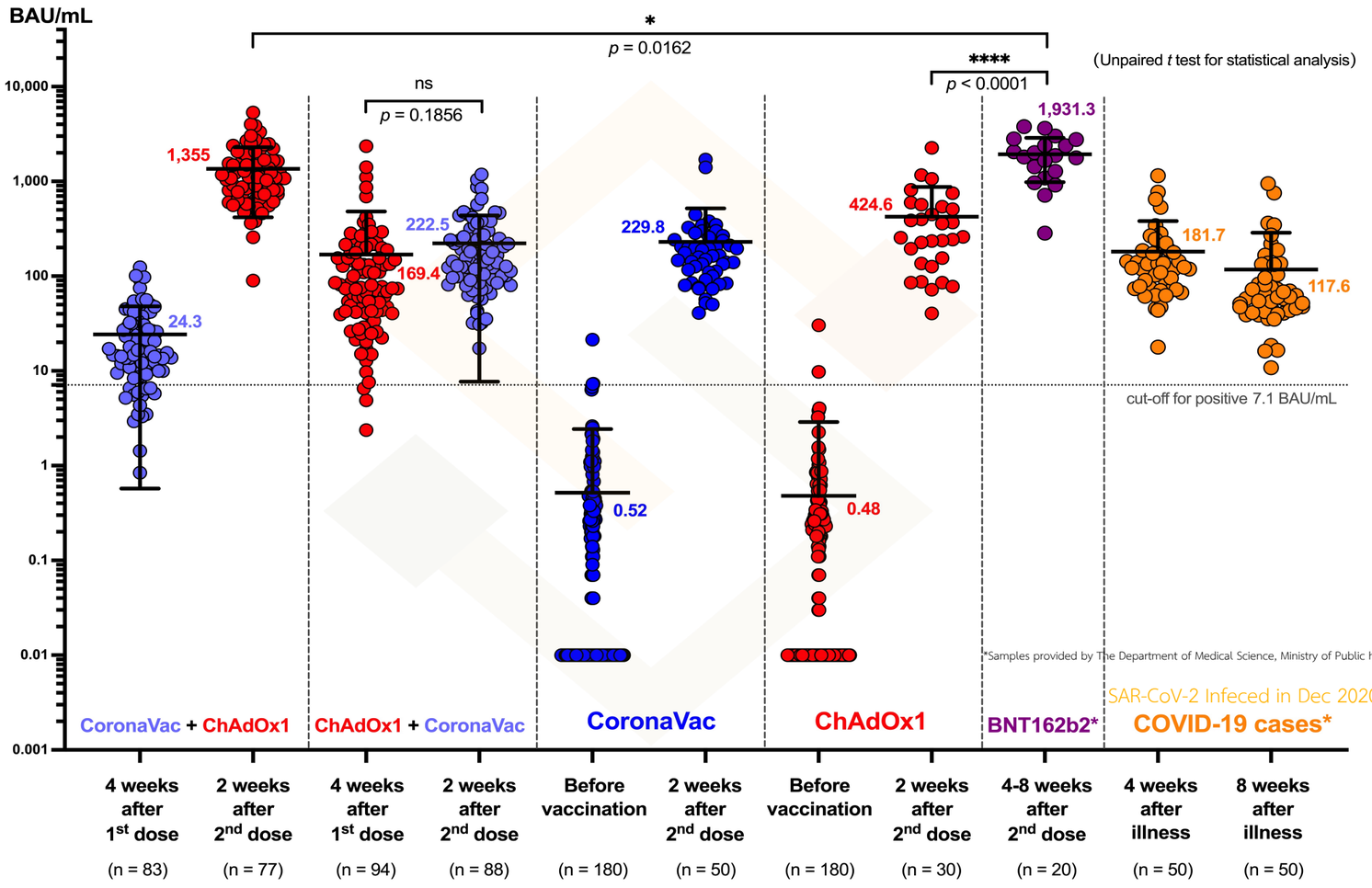


Figure 1. Anti-RBD IgG antibody against SAR-CoV-2 by CMIA

**Method:** This prospective study conducted in healthy volunteers who were assigned to receive either CoronaVac (1st dose) followed by ChAdOx1 (2nd dose) or ChAdOx1 followed by CoronaVac in 1:1 ratio. Adverse events were self-reported for 7 days post-vaccination. Anti-receptor binding domain (RBD) IgG antibody titers were measured by chemiluminescent microparticle immunoassay (CMIA; Abbott Laboratories, Ltd.) at day 28 (on the day of the 2nd vaccination), day 42, and day 90 after the first vaccination. Thirty participants from each group were randomly selected to test for 50% plaque reduction neutralization antibody assay against SARS-CoV-2 delta strain live virus ($PRNT_{50}$).

**Results**: Both assays for anti-RBD IgG (Fig 1) and $PRNT_{50}$ against delta variant (Fig 2) revealed that heterologous vaccination with CoronaVac followed by ChAdOx1 (CoronaVac-ChAdOx1) induced significantly higher geometric mean titer (GMT) than the reverse sequence (ChAdOx1-CoronaVac), and significantly higher than homologous vaccination of CoronaVac-CoronaVac, and notably higher than ChAdOx1-ChAdOx1. However, the $PRNT_{50}$ from CoronaVac-ChAdOx1 was lower than the homologous vaccination with the BNT162b2 mRNA vaccine or the convalescent sera from those recovered from delta infection. The adverse events were less common following CoronaVac than ChAdOx1. There was not serious adverse event.

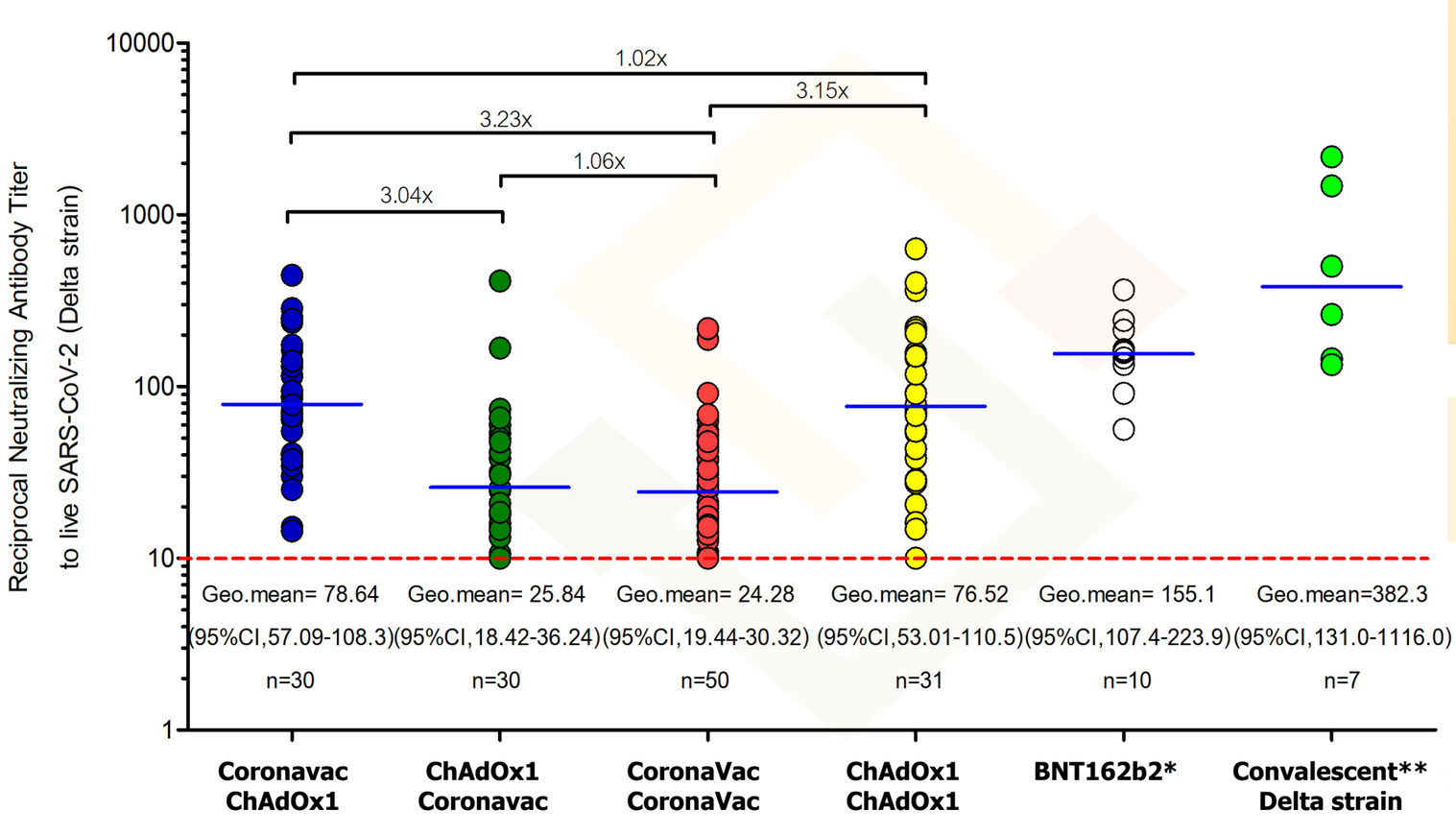


Figure 2. 50% plaque reduction neutralization against delta variant

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