DURABILITY AND BOOSTABILITY OF Ad26.COV2.S IN RHESUS MACAQUES

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BACKGROUND

Ad26.COV2.S is a single-shot vaccine that has demonstrated clinical efficacy against symptomatic COVID-19. In this study, we report the durability of immune responses in rhesus macaques received single-shot Ad26.COV2.S and the immunogenicity of a booster shot at 8-10 months following the initial immunization.

METHODS

Animals were immunized by intramuscular route with 10^{11} vp (N=10) or $5x10^{10}$ vp (N=10) Ad26.COV2.S and were followed for either 230 or 315 days. Animals were then boosted with $5x10^{10}$ vp Ad26.COV2.S (N=10). Humoral immune responses including RBD-specific Ig ELISA and pseudovirus-based virus neutralization assay were monitored. Circulating RBD-specific memory B cells and bone marrow plasma cells were assessed by multiparameter flow cytometry.

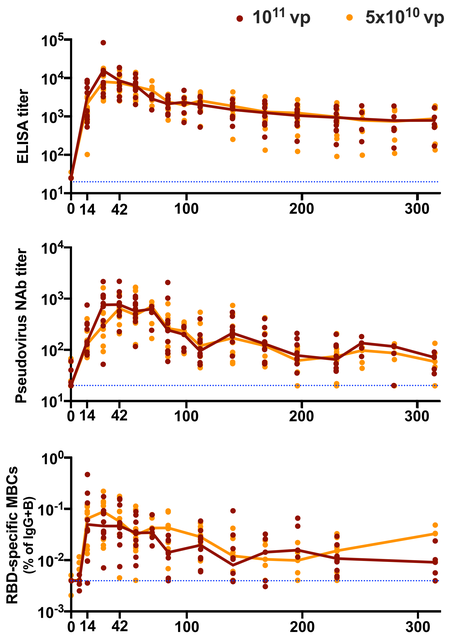


Figure 1

Ad26.COV2.S vaccination generates durable antibody and B cell immune responses which are enhanced by homologous booster in macaques

RESULTS

Ad26.COV2.S elicited robust and comparable RBD-specific binding and neutralizing antibody responses in animals that received the 10^{11} vp and $5x10^{10}$ vp doses, which peaked on days 28-56. All animals showed binding antibody responses for the duration of follow-up, and 17 of 20 animals showed neutralizing antibody responses by day 230-315 (Fig.1). RBD-specific memory B cell response peaked on day 14-28 followed by a gradual decline, and remained detectable in 17 of 20 animals by day 230-315 (Fig.2). On day 315 following vaccination, bone marrow RBD-specific PCs were detected in the majority of vaccinated macaques, and correlated with antibody responses (Fig.2). Following Ad26.COV2.S boost immunization, RBD-specific binding antibody responses increased 31-69 fold compared with pre-boost levels against the ancestral (WA1/2020), alpha (B.1.1.7), beta (B.1.351), kappa (B.1.617.1), and delta (B.1.617.2) SARS-CoV-2 variants (Fig.3). Neutralizing antibody responses increased 23-43 fold compared with pre-boost levels against the ancestral, alpha, beta, gamma (P.1), kappa, and delta SARS-CoV-2 variants (Fig.3). Antigen-specific memory B cell response also increased 8 fold following the boost immunization (data not shown).

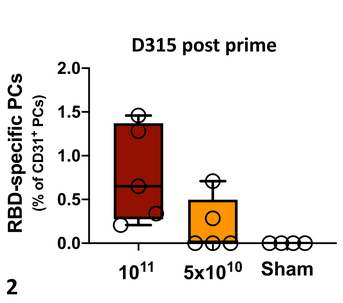
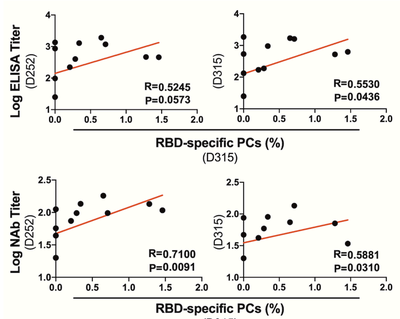


Figure 2



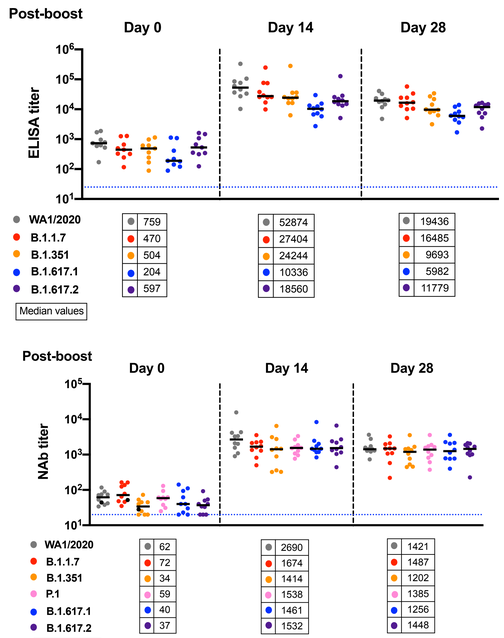


Figure 3

CONCLUSIONS

Ad26.COV2.S elicited durable antibody and B cell responses, and a late boost with Ad26.COV2.S resulted in a dramatic increase in humoral immunity that were highly cross-reactive across multiple SARS-CoV-2 variants in rhesus macaques. These data contribute to our understanding of Ad26.COV2.S durability and the benefit of boosting in macaques and support current clinical recommendations for Ad26.COV2.S boosting in humans.

ADDITIONAL KEY INFORMATION

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