Humoral immune responses to ancestral SARS-CoV-2 wild type and variant strains following COVID-19 vaccination in people with HIV

David W.J. Griffin,[1] Irene Boo,[2,3,4] Shir Sun, [5,6] Anna Coldham,[1] Heidi E. Drummer, [2,3,4] Menno C. van Zelm, [5,6] James H. McMahon[1]

[1]Department of Infectious Diseases, Alfred Health and Monash University; [2]Viral Entry and Vaccines Group, Burnet Institute, Melbourne, VIC, Australia; [3]Department of Microbiology and Immunology, Peter Doherty Institute for Infection and Immunity, University of Melbourne, Melbourne, VIC, Australia; [4]Department of Microbiology, Monash University, Clayton, VIC, Australia; [5]Department of Immunology, Monash University, Melbourne, VIC, Australia; [6]Allergy, Asthma and Clinical Immunology Service, Alfred Hospital, Melbourne, VIC, Australia

Background: People with HIV (PWHIV) have reduced humoral immune responses to multiple vaccines compared to people without HIV. In addition, SARS-CoV-2 variants of concern (VoC) have the potential to evade immunity provided by COVID-19 vaccines targeting wild type virus. We sought to describe humoral immunity to ancestral SARS-CoV-2 and multiple VoCs in PWHIV after 2 and 3-dose courses of COVID-19 vaccine.

Methods: We prospectively recruited PWHIV receiving antiretroviral therapy, and collected blood samples before commencing vaccination, at 1- and 6-months after the second dose, and 1-month after the 3rd vaccine dose**.** We measured SARS-CoV-2 receptor binding domain (RBD) and nucleocapsid IgG responses by an ELISA (microg/mL) and neutralising antibodies (nAb) against ancestral SARS-CoV-2 virus, Delta, and Omicron (BA.2, and BA.4/5) variants in a pseudovirus assay expressed as the dilution of plasma required to inhibit 50% viral entry (ID50)

Results: We enrolled 22 PWHIV (95% male, median age 50.6 [IQR 43.4-58.9]) on antiretroviral therapy. Eleven received mRNA vaccines for their primary and first booster doses. The median concentration of RBD-specific IgG was 21.7 (IQR 4.6-38.2) microg/mL after two, and 61.2 (IQR 54.7-83.3) microg/mL after three doses of COVID-19 vaccine. Recipients of two mRNA vaccine doses had higher concentration of RBD-specific IgG (39.9 microg/mL, IQR 17.1-44.2) than those receiving a primary schedule of adenoviral vector vaccines (16.8 microg/mL, IQR 9.7-23.6). While ancestral COVID-19 vaccines generate robust nAb responses in PWHIV to wild type and Delta variants, nAb titres to BA.2, and BA.4/5 were reduced.

Conclusion: PWHIV on antiretroviral therapy mount serological responses to COVID-19 vaccines, which increased after a third dose. Neutralisation of contemporary COVID-19 variants is poorer than against wildtype and Delta strains, following ancestral vaccination. More data are needed to better understand the role of additional booster doses, particularly with bivalent COVID-19 vaccines, to enhance humoral immunity to circulating COVID-19 variants.