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ChAdOx1 nCov-19 VACCINATION IN PWH: IMMUNE RESPONSES TO SARS-CoV-2, VOCs and HCoVs

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BACKGROUND

People living with HIV (PWH) may represent a high-risk group for adverse clinical outcomes from SARS-CoV-2. The duration of protection from SARS-CoV-2 and emerging variants of concern (VOC) in PWH following vaccination is unclear. Furthermore, the role of pre-existing SARS-CoV-2 immune responses, likely acquired from prior exposure to circulating human coronaviruses (HCoVs), on vaccine-mediated immunity remains to be determined. Understanding the kinetics of immune responses to SARS-CoV-2 and VOCs, and the impact of pre-existing SARS-CoV-2 immunity on vaccine-mediated immune responses will be critical in informing COVID-19 vaccination policies in PWH.

METHODS

Study Cohort: HIV+ male volunteers (on ART, VL undetectable, CD4+ T cells >350 cells/ul) and 50 HIV- controls were recruited in this open-label non-randomised sub-study within the phase 2/3 COV002 trials (clinical trial ID: NCT04400838). Participants received the ChAdOx1 nCoV-19 vaccine according to the schedule below (Figure 1)

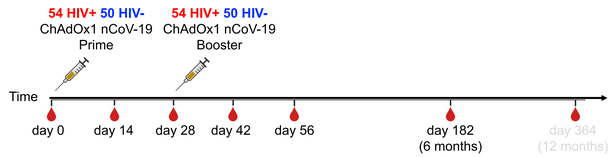

Figure 1: Vaccination schedule for HIV+ sub-study within COV002 clinicals trial trial

Immunophenotyping: Expression levels of markers of immune activation, exhaustion and phenotype were measured ex vivo from cryopreserved PBMC using flow cytometric panels.

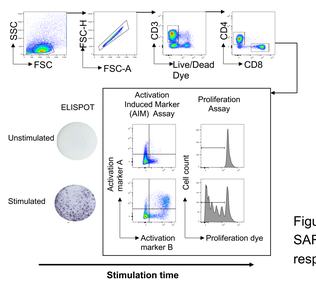

Figure 2: T cell assays for measuring SARS-CoV-2 and CCC-specific responses including ELISPOT

Immune response to vaccination and CCC: Humoral immunity was measured using ELISA (MSD and an in-house) while cellular immunity was measured using a selection of T cell assays (Figure 2).

PWH make **robust** and **durable humoral** and **cellular** immune responses to **SARS-CoV-2 and VOCs** for up to 6 months following **ChAdOx1 nCoV-19 vaccination**, and these responses are **modulated** by **previous exposure** to **β-coronaviruses**

RESULTS

1. Persistent immune activation and phenotypic exhaustion in PWH before and after vaccination

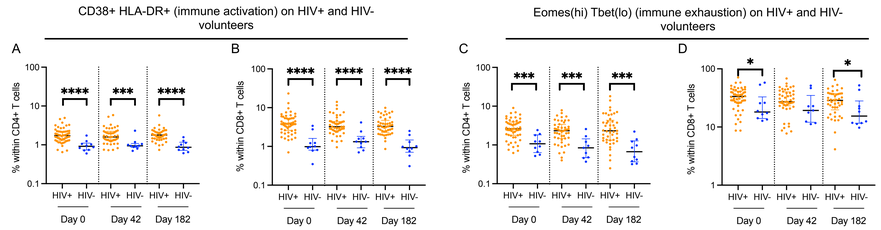

Figure 3: Frequency of markers of immune activation CD38+ HLA-DR+ on (A) CD4+ and (B) CD8+ T cells in HIV+ (orange) and HIV- (blue) volunteers. Phenotypic exhaustion as measured by Eomes (hi) Tbet (lo) on (C) CD4+ and (D) CD8+ T cells in HIV+ (orange) and HIV- (blue) volunteers.

2. ChAdOx1 nCoV-19 vaccination induces potent and durable humoral immunity against SARS-CoV-2 and VOC

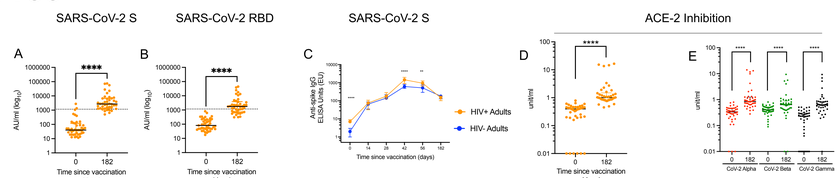

Figure 4: Levels of SARS-CoV-2 (A) spike and (B) RBD antibodies in plasma of ChAdOx1 nCoV-19 vaccinated HIV+ volunteers. (C) Longitudinal analysis of antibody kinetics following vaccination in HIV+ and HIV- volunteers. (D) ACE-2 inhibition as surrogate for antibody neutralisation function showing higher levels of neutralising antibody against SARS-CoV-2 and variants of concern (VOCs) 6 months following vaccination

3. Durable SARS-CoV-2-specific T cell responses are induced following ChAdOx1 nCoV-19 vaccination

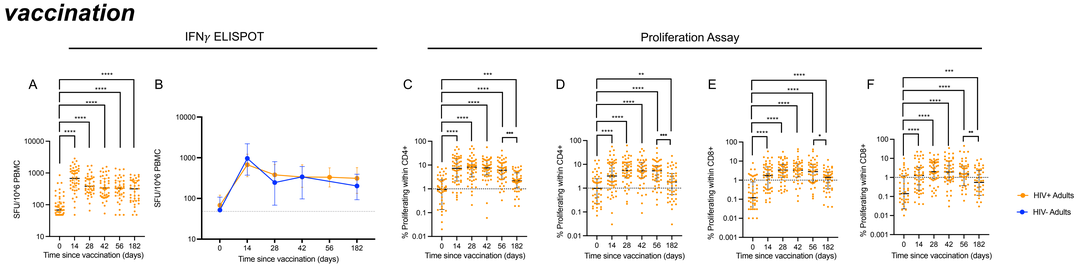

Figure 5: Kinetics of T cell response measured using overlapping peptide (OLPs) pools for SARS-CoV-2 spike protein by (A) IFNγ ELISPOT in vaccinees followed for 6 months. (B) IFNγ ELISPOT in HIV+ and HIV- volunteers over 6 months. Longitudinal analysis of T cell response measured following stimulation with OLPs targeting (C) SARS-CoV-2 S1, (D) SARS-CoV-2 S2 in CD4+ and (E) SARS-CoV-2 S1, (F) SARS-CoV-2 S2 in CD8+ in T cell proliferation assay.

4. Responses to variants of concerns (VOCs) are preserved up to 6 months after vaccination

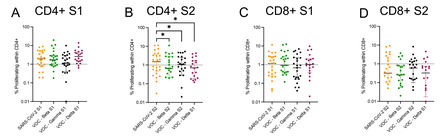

Figure 6: CD4+ T cell responses to SARS-CoV-2 and VOC (A) S1, (B) S2. CD8+ T cell responses to SARS-CoV-2 and VOC (C) S1 and (D) S2 6 months following vaccination of PWH

5. SARS-CoV-2-specific T cells are not differentially biased towards CD4 T cell subsets

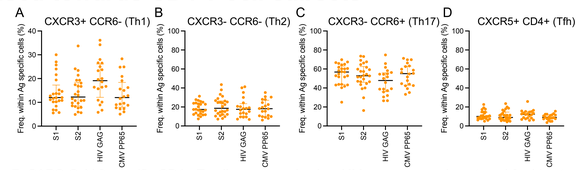

Figure 7: SARS-CoV-2 specific CD4+ T cells measured using AIM assay were phenotyped for bias towards (A) Th1 (B) Th2, (C) Th17 and (D) Tfh cells using chemokine receptors CXCR3, CXCR5 and CCR6.

6. Pre-existing cross-reactive CCC responses modulate SARS-CoV-2 post-vaccination responses

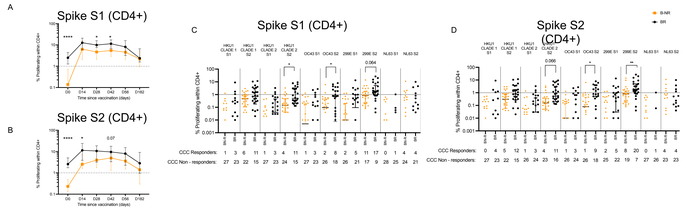

Figure 8: Longitudinal analysis of SARS-CoV-2-specific responses in PWH with pre-existing, cross-reactive immune responses measured at baseline (black, BR) compared with those without (yellow line, B-NR) to (A) S1 and (B) S2 in CD4+ T cells. Baseline CD4+ T cells responses to endemic CCC (C) S1, (D) S2 proteins in endemic CCCs are measured at baseline in BR and B-NR. Similar observations were made in CD8+ T cells (not shown)

CONCLUSIONS

- In PWH, ChAdOx1 nCoV-19 vaccination induces potent T and antibody immune responses at levels comparable to HIV uninfected volunteers.
- ChAdOx1 nCoV-19 vaccine-induced responses were present 6 months post-vaccination although there is evidence of waning immune response underscoring a need for boosters for PWH.
- Pre-existing cross-reactive T cell response to CCC induce higher magnitude post-vaccination responses.

ADDITIONAL KEY INFORMATION

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