RBDCOV Project

T-cell Immunity of PHH-1V COVID-19 Vaccine in PWH and Adults with Immunosuppressive Conditions

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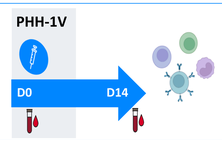
BACKGROUND

Protective vaccines became an urgent need during the COVID-19 pandemic. People with immunodeficiencies particularly benefit from COVID-19 vaccination. PHH-1V (BIMERVAX®) is an authorized, adjuvanted recombinant protein vaccine based on a Beta/Alpha receptor-binding domain (RBD) heterodimer of SARS-CoV-2 (1,2). The HIPRA-HH-4 study (NCT05303402) evaluated the immunogenicity and safety of the PHH-1V booster in participants with HIV (PWH) and other immunodeficiencies who are considered at higher risk of adverse COVID-19 outcomes compared to the general population. Here, we evaluate the cellular immune response elicited by the PHH-1V booster in individuals with 5 different immunosuppressive conditions (IC).

METHODS

The HIPRA-HH-4 study was a Phase IIb/III, open-label, single-arm, multi-center study (NCT05303402). Participants included adults aged **18** to **76** years who were **primarily vaccinated with mRNA virus vaccines**.

SARS-CoV-2 specific T-cell responses were analyzed in peripheral blood mononuclear cells at baseline (D0) and day 14 (D14) after PHH-1V booster.



Using 15-mer overlapping peptide pools covering the RBD region of **Wuhan** (D614G), B.1.351 (**Beta**; vaccine-matched), B.1.617.2 (**Delta**), Omicron **BA.1**, and Omicron **BA.2** SARS-CoV-2 variants.

Total T-cell responses were measured by **IFNγ+ ELISpot.**

IFNγ+ and IL2+ cytokine-mediated CD4+ and CD8+ T-cell responses were measured by **intracellular cytokine staining.**

We analyzed the cellular immune response after PHH-1V booster vaccination in cryopreserved peripheral blood mononuclear cells (PBMCs) samples at baseline (D0) and day 14 (D14) post-vaccination across 5 IC groups: PWH (n=30) and participants with kidney transplant under anti-rejection therapy with immunosuppressive drugs (KTx, n=23), kidney disease on hemodialysis (HD, n=26), primary antibody deficiency disorders (PAD, n=18), and autoimmune diseases on treatment with rituximab/ocrelizumab (AID, n=44). We measured the total magnitude and functionality of T-cell responses by IFNγ ELISpot and intracellular cytokine staining (ICS) assays, respectively. Mixed-effects models were used on squared root-transformed data, stratified by sex.

The PHH-1V booster vaccination enhances cellular immunity against SARS-CoV-2 in people with HIV and a broad range of individuals with immunosuppressive conditions, primarily promoting the expansion of the IFNγ+CD4+ T-cell phenotype across study groups

RESULTS

	PWH			KTx			HD			PAD			AID		
In vitro stimulation	All	Prior COVID	No Prior COVID	All	Prior COVID	No Prior COVID	All	Prior COVID	No Prior COVID	All	Prior COVID	No Prior COVID	All	Prior COVID	No Prior COVID
Wuhan	IFNγ Tc IFNγ⁺CD4⁺	IFNγ Tc IFNγ⁺CD4⁺	IFNγ Tc	-	-	-	IFNγ Tc IFNγ⁺CD4⁺	IFNγ Tc IFNγ⁺CD4⁺	-	IFNγ Tc	-	-	IFNγ Tc IFNγ⁺CD4⁺	-	-
Beta	IFNγ Tc IFNγ⁺CD4⁺ IFNγ⁺CD8⁺	IFNγ Tc IFNγ⁺CD4⁺	-	IFNγ⁺CD4⁺	-	-	IFNγ Tc	IFNγ Tc	IL2⁺CD4⁺	IFNγ Tc	IFNγ Tc	-	-	-	IFNγ Tc
Delta	IFNγ Tc	IFNγ Tc	-	-	-	-	-	-	-	-	-	-	IFNγ⁺CD4⁺	-	IFNγ⁺CD4⁺
Omicron BA.1	IFNγ Tc IFNγ⁺CD4⁺	IFNγ⁺CD4⁺	IFNγ⁺CD8⁺	-	-	-	IFNγ⁺CD4⁺	IFNγ Tc	IL2⁺CD4⁺	IFNγ Tc	-	-	-	-	-
Omicron BA.2	IFNγ Tc	IFNγ Tc IFNγ⁺CD4⁺	-	-	-	-	IFNγ⁺CD4⁺ IL2⁺CD8⁺	IFNγ⁺CD4⁺	-	IFNγ⁺IL2⁺CD4⁺	IFNγ⁺IL2⁺CD4⁺	-	-	IFNγ⁺IL2⁺CD4⁺	-

Table 1. Summary of the significant differences in the T-cell response between D0 and D14 (post-vaccine booster) by ELISpot and ICS of participants with IC. The table shows significant (p<0.05) increases of the percentage of T cells, as determined by ELISpot (IFNγ+ Tc) and ICS (IFNγ+IL2+CD4+, IFNγ+CD4+, IL2+CD4+, IFNγ+IL2+CD8+, IFNγ+CD8+, IL2+CD8+), for each *in vitro* stimulation of PBMCs with peptide pools covering the RBD of the Wuhan, Beta, Delta, Omicron BA.1, and Omicron BA.2 SARS-CoV-2 variants. Statistical analyses were performed using data from all participants (All) or separately from those who had a previous SARS-CoV-2 infection (Prior COVID) and those who did not (No Prior COVID). AID, people with autoimmune diseases; D0, day 0 (baseline); D14, day 14; PWH, people with HIV; HD, people on hemodialysis; IC, immunosuppressive conditions; ICS, intracellular cytokine staining; KTx, people with kidney transplant; PAD, people with primary antibody deficiency disorders; PBMCs, peripheral blood mononuclear cells; RBD, receptor-binding domain; Tc, T cell.

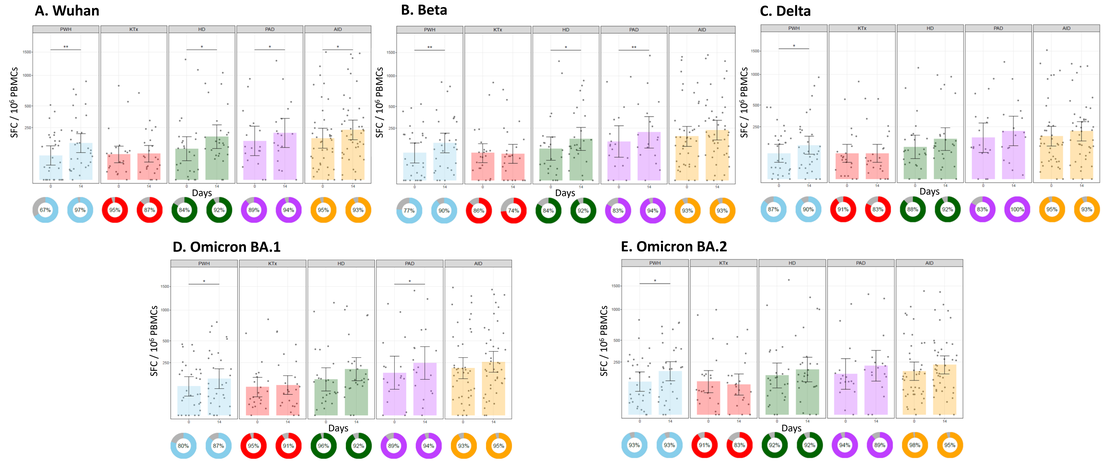


Figure 1. T-cell response by IFNγ ELISpot following stimulation of PBMCs from all participants with peptide pools covering the RBD of the Wuhan **(A)**, Beta **(B)**, Delta **(C)**, Omicron BA.1 **(D)**, and Omicron BA.2 **(E)** SARS-CoV-2 variants. Bar graphs show the adjusted treatment mean counts (95% CI) of IFNγ+ T cells per million PBMCs on D0 and D14 after boosting with PHH-1V. The pie charts below show the percentage of responder subjects at each time point. AID, people with autoimmune diseases; CI, confidence interval; D0, day 0 (baseline); D14, day 14; HD, people on hemodialysis; KTx, people with kidney transplant; PAD, people with primary antibody deficiency disorders; PBMCs, peripheral blood mononuclear cells; PWH, people with HIV; RBD, receptor-binding domain; SFC, spot-forming cells. *: p<0.05, **: p<0.01.

CONCLUSIONS

- Except in KTx, the PHH-1V booster administered to participants with IC expands specific T-cell populations, mainly those with the IFNγ+CD4+ phenotype. Specifically, the significant increases in IFN-γ T-cell responses observed in PWH and participants with HD who had been previously infected with the virus suggest that the PHH-1V booster primarily recalls memory T cells established by prior SARS-CoV-2 infection and vaccination.
- The PHH-1V booster elicited little to no T-cell response in patients with KTx, possibly due to their anti-rejection therapy.
- Participants with HIV showed the broadest T-cell response across all the tested SARS-CoV-2 variants.

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ADDITIONAL KEY INFORMATION

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