Humoral immunity after PHH-1V COVID-19 booster vaccination in adults with immunosuppressive conditions

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INTRODUCTION

Individuals with immunosuppressive conditions are at high risk of developing SARS-CoV-2–associated complications and face death, and their responses to vaccination widely vary upon the underlying immune impairment.

PHH-1V is an authorized adjuvanted recombinant protein vaccine based on a dimeric receptor binding domain (RBD) of Alpha and Beta SARS-CoV-2 variants, to boost immunogenicity in adult individuals.

OBJECTIVES

To evaluate humoral immune responses in 5 groups of immunosuppression:

- People living with HIV (**PWH**, <400 $CD4^+$ T-cells/mm^3)
- Recipients of kidney transplant (**KTx**)
- Patients on chronic hemodialysis (**HD**)
- Patients with primary antibody deficiencies (**PAD**)
- Patients with autoimmune diseases on anti-CD20 therapy (**AID**)

METHODS

HIPRA-HH4 study (NCT05303402): phase IIb/III, open label, single arm, and multi-centre trial.

238 individuals with previous mRNA vaccination and boosted with PHH-1V, were included from 3 sites in Spain.

Humoral responses were analyzed in serum samples at baseline (D0) and at 14 days (D14) after PHH-1V booster using Virus or Pseudovirus neutralization assays against different viral variants (neutralizing antibodies, nAb) and an electrochemiluminescence immunoassay (binding antibodies).

Mixed effects models were used on log transformed data including the visit, COVID-19 history and age (≥18 to <65 years; ≥65 years) as fixed effects.

Results are reported as geometric mean titre fold rise (GMFR) and 95% confidence interval.

Cellular immune responses were also assessed (not shown here).

	PWH (N=61)	KTx Tx (n=37)	HD (n=59)	PAD (n=24)	AID (n=57)	TOTAL (n=238)
Age (years), median (IQR)	55 (26-75)	55 (21-74)	71 (26-90)	50 (27-86)	56 (25-78)	**56 (21-90)**
Sex, ♂/ ♀ (%)	79/21	81/19	75/25	54/46	30/70	**64/36**
CD4 T cell count cells/mm^3, mean (SD)	260 (130)	420 (230)	590 (240)	650 (320)	850 (420)	**550 (350)**
Prior COVID-19, n (%)	34 (56%)	17 (46%)	30 (51%)	19 (79%)	27 (47%)	**127 (53%)**

Table 1. Baseline characteristics of study population.

RESULTS

From D0 to D14 **total anti-RBD binding antibodies** increased in all immunosuppressive conditions, GMFR between 7.2 (5.6, 9.3) in **PWH** and 2.3 (1.6, 3.4) in **PAD**, except for individuals with **AID** [GMFR 1.2 (1.0, 1.6)].

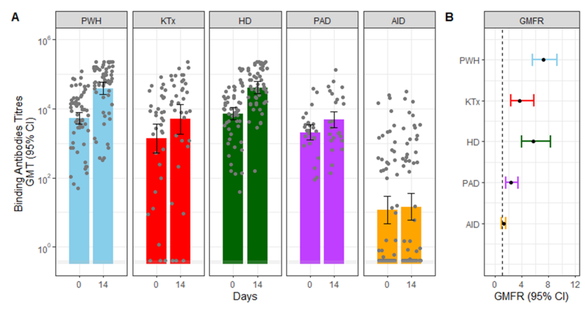

Figure 1. Total anti-RBD binding antibody titers at baseline and at day 14 (A) and the corresponding fold-rise (B) for the overall participants.

Boosting of nAb against BA.2 variant in **PWH** [GMFR 4.5 (5, 5.8)] was comparable to the **HD** group [GMFR 5.6 (3.7, 8.5)] and higher than in **KTx**, **PAD** and **AID** (GMFR between 2.6 and 1.2), similarly to D614G nAb.

For BA.1, BA.4-5 and BETA variants, the rise of nAb in **HD** (GMFR range 7.8 – 5.5) was higher than in **KTx** (GMFR range 4.7 – 3.1) and **PAD** (GMFR range 3.0 – 1.7), and not significant for **AID** (GMFR range 1.4 – 1-2).

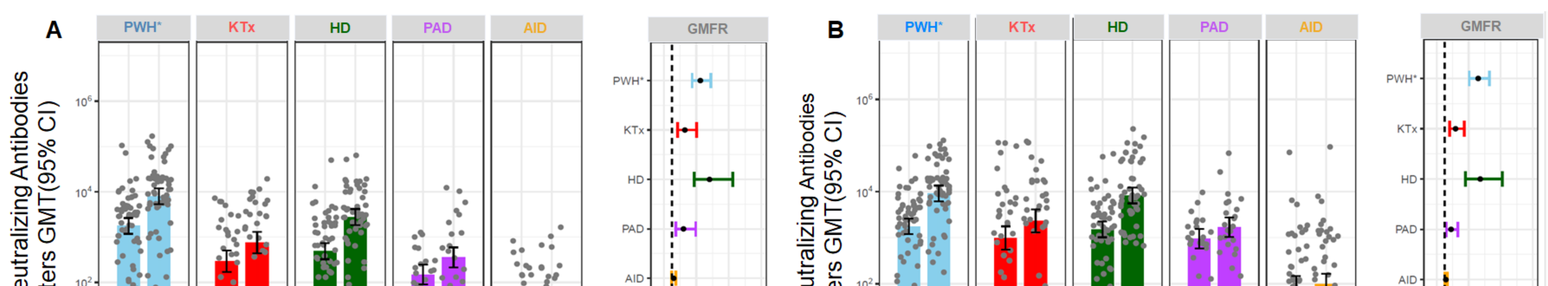

Figure 2. Neutralizing antibody response from all participants. A) Variant BA.2; B) Variant D614G. *PWH tested in VNA (Virus Neutralization Assay)

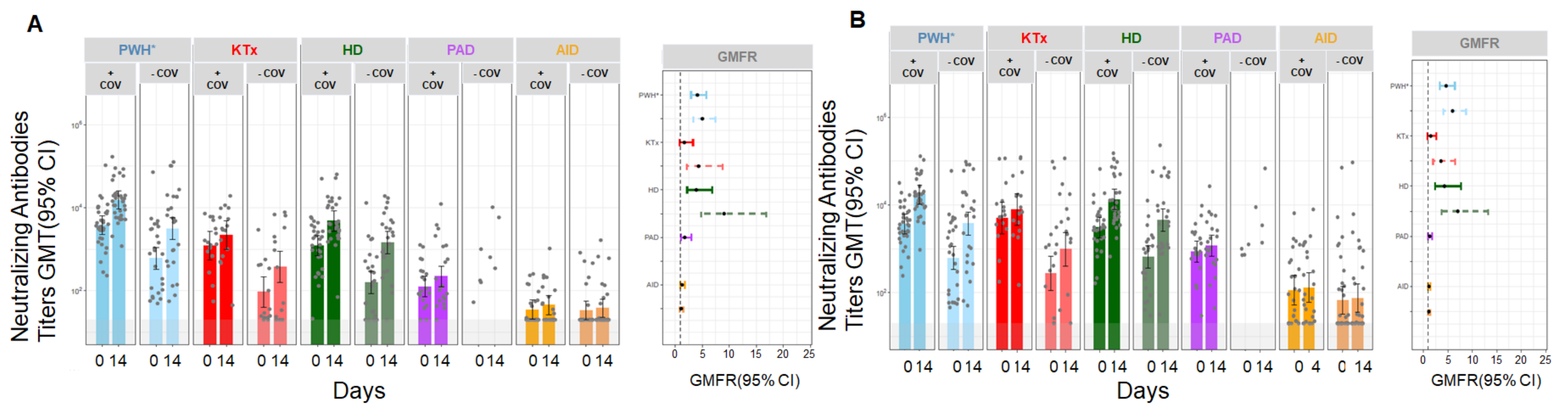

Figure 3. Neutralizing antibody response from participants with (+COV) or without (-COV) previous SARS-CoV-2 infection. A) Variant BA.2; B) Variant D614G. *PWH tested in VNA (Virus Neutralization Assay)

CONCLUSION

PHH-1V booster vaccination elicited significant increases in total binding antibodies and neutralizing titers between D0 and D14 in **PWH** with <400 CD4 T-cells/mm3, **KTx**, **HD** and **PAD** but not the **AID** group due to the anti-CD20 therapy. These findings were independent of prior COVID-19 episodes.

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