RBDCOV Project

#425

Studying humoral and cellular responses of RBD, receptor binding domain, based Covid-19 vaccine: A study of 5 groups of individuals with immunosuppressive conditions.

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Background

Individuals with immunosuppressive conditions are at high risk of developing SARS-CoV-2–associated consequences and death, and their responses to vaccination widely vary upon the underlying immune impairment. PHH-1V is an adjuvated recombinant vaccine based on a dimeric RBD of two SARS-CoV-2 variants (alpha and Beta), to boost immunogenicity in ≥16 years old.

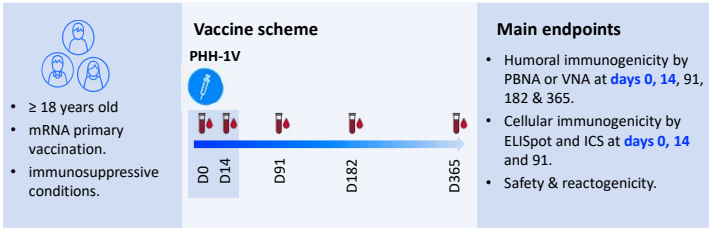
Objectives

To evaluate the immune response elicited by the PHH-1V booster vaccination in participants with 5 different types of immunosuppressive conditions.

Methods

HIPRA-HH4 study (NCT05303402): phase IIb/III, open label, single arm, multi-centre, trial. Participants with mRNA primary vaccination and immunosuppressive conditionswere included:

- People with HIV and CD4 < 400 cells/ml (***PWH***, n=61).
- Kidney transplant under ≥ 3 immunosuppressive drugs (***KTx***, n=37)
- Renal disease on chronic dialysis (***HD***, n=59)
- Primary immunodeficiency on IgG substitution therapy (***PAD***, n=24)
- Autoimmune disease on anti-CD20 therapy, Rituximab® (**AID**, n=57).



Humoral and cellular immune response were measured by PBNA or VNA and, ELISpot and ICS assays respectively against Omicron BA.1 and BA.2, as the dominant variant at inclusion.

Results

238 participants with median age of 56 years old were enrolled and boosted with PHH-1V.

Table 1: Baseline characteristics

	PWH (N=61)	Kidney Tx (n=37)	HD (n=59)	PAD (n=24)	AID on αCD20 (n=57)	TOTAL (n=238)
Age (years)	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**
Prior COVID-19 ; n (%)	34 (56%)	17 (46%)	30 (51%)	19 (79%)	27 (47%)	**127 (53%)**

PHH-1V booster induced a significant increase at day 14 compared to baseline against both variants in PWH, KTx and HD, a moderate increase on PAD, but no effect on the AID group.

Significant increases in the frequency of IFNγ⁺ T cells were detected in the PWH, HD and PAD groups by ELISpot and/or ICS, that not reached statistically significance in the AID group.

On the contrary, no increases were observed in the KTx group, which is consistent with their anti-rejection therapy.

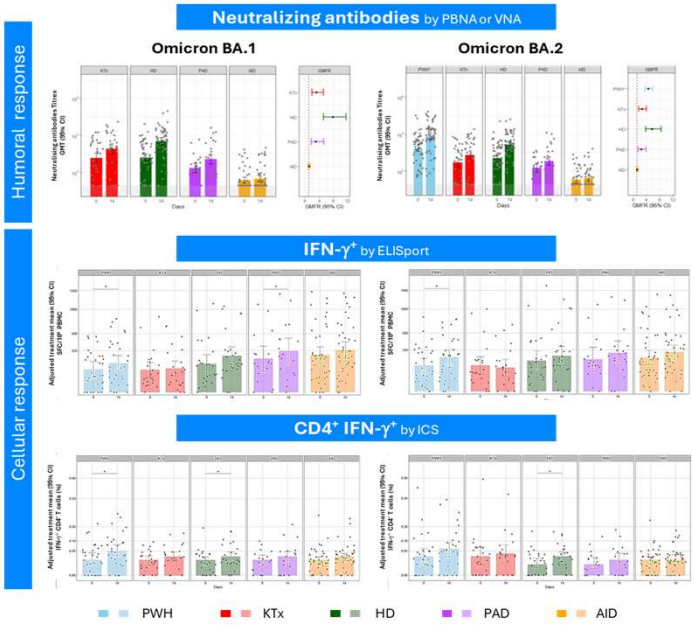


Figure 1: Humoral and cellular response against SARS-CoV2 variants at day 14 after PHH-1V booster in immunocompromised groups. (Top panel) GMT for adjusted treatment mean (95% CI) at baseline and day 14 after booster (*left panel*) and GMFR for adjusted value at day 14 compared to base line (*right panel*). **(Middle).** IFN-γ producing T cells upon PBMC re-stimulation with SARS-CoV-2 derived peptide pools. Adjusted treatment mean (95% CI). **(Bottom).** IFN-γ⁺CD4⁺ T cells upon PBMC re-stimulation with SARS-CoV-2 derived peptide pools. Adjusted treatment mean and its 95% CI.*: P<0.05, **: P<0.01

Overview of the immune response to the PHH-1V booster in different participant groups:

- **PWH and HD:** The PHH-1V booster induces a clear humoral (antibody) and cellular (T-cell) response in these groups.
- **KTx Individuals** show a moderate humoral response, but no consistent cellular response, likely due to the immunosuppressive effects of anti-rejection drugs on T-cells.
- **PAD Group**: Moderate increase in humoral response. Significant increase in cellular response, suggesting a compensatory immunological effect from T-cells.
- **AID Group**: No humoral response due to the B cell effect of anti-CD20 (Rituximab®) treatment. Slight compensation in cellular response with moderate IFN-γ producing cells

Conclusions

PHH-1V booster vaccination elicits both humoral and cellular immune response against SARS-CoV-2 on a broad range of individuals with immunosuppressive conditions. The response level and type varies according to the underlying condition and/or its associated treatment.

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