Three Doses of COVID-19 Vaccines in PWH: Immunogenicity and Effects on HIV Reservoir

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BACKGROUND

- We aim to understand whether older PWH can develop strong and lasting immunity across different arms of the immune system in response to COVID-19 vaccines without adverse reactions from HIV reservoirs.

Older people with HIV (PWH) have a higher risk of complications from SARS-CoV-2 due to immunosenescence and potential immunodeficiency caused by HIV. It is unclear, however, whether COVID-19 vaccines with a booster (3 doses, D1-3) elicit strong and lasting immunity in this population, or whether they can destabilize HIV reservoirs.

METHODS

- **Participants:** 68 PWH on cART, ≥ 55 y.o. (immune responders, IR; immune non-responders, INR; low-level viremia, LLV; long-term non-progressors, LTNP); 23 HIV-negative ≥ 55 y.o. (**Fig. 1**).
- **Samples:** blood (serum, PBMC), saliva.
- **Analyses:** Spike/RBD Abs, nAbs (ELISA, snELISA); NT50 (microneutralization); RBD/NTD B cells (spectral flow cytometry); anti-Spike T-cells (ELISpot); HIV reservoirs (IPDA, ELISpot); clinical.

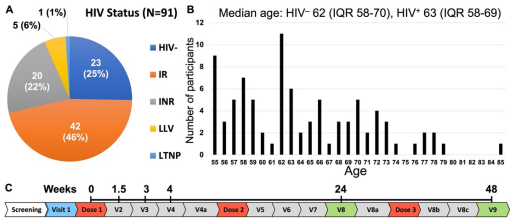

Fig. 1. Study participants by HIV status **(A)**; age distribution **(B)**; the study timeline **(C)**.

RESULTS

Vaccines elicited equally strong anti-Spike IgG in PWH and HIV⁻ in serum and saliva (not shown), and RBD IgG in serum (**Fig. 2**). Serum Abs peaked at 4 weeks post-D3. Week 48 serum IgG in PWH vs HIV⁻ were 916 vs 919 BAU/mL for Spike (p=0.624) and 706 vs 752 for RBD (p=0.198), respectively.

COVID-19 vaccine booster is essential for protection in PWH, does not destabilize HIV reservoirs, but may pose risk in unsuppressed viremia.

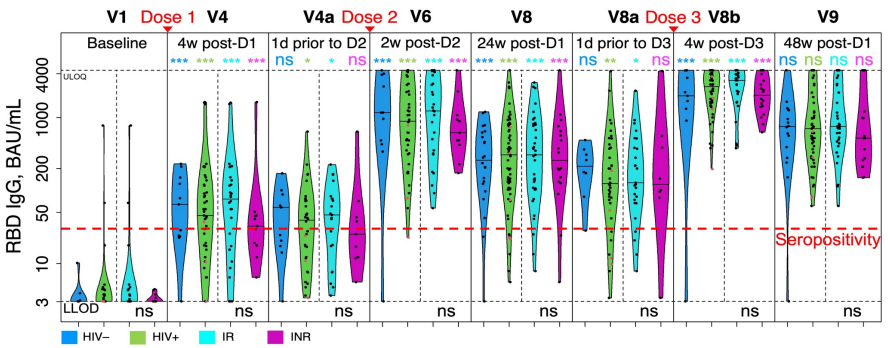

Fig. 2. Changes in levels of serum IgG to Spike RBD following COVID-19 vaccination from Baseline through V9 (48 weeks after Dose 1).

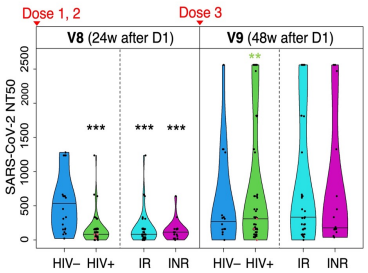

Fig. 3. SARS-CoV-2 NT50 titers at 24 weeks (V8) – after 2 vaccine doses, and 48 weeks (V9) – after 3 doses.

Median neutralizing titers post-D2 were significantly lower in PWH than in HIV⁻ (NT50 82.9 vs 535, p<0.001). After D3, at 48 weeks, PWH had similar titers: 309 vs 269 (**Fig. 3**).

Anti-Spike T cell cytokine responses were stronger in IR PWH after D2 and D3 than in HIV⁻ (**Fig. 4**). Week 48 anti-Spike IL-2 responses: median 135 SFC/10^6 PBMC vs 43.8 (p<0.001), but only 12.5 in INR (p=0.001 vs IR).

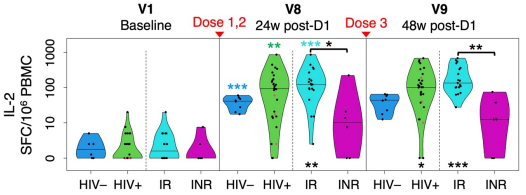

Fig. 4. Frequency of IL-2-secreting anti-Spike T cells at 24.

Vaccines did not affect the size of the HIV reservoir in PWH (**Fig. 5**). The change in median frequency of intact proviruses from baseline: 95.0 vs 90.9 (p=0.952), except in three LLV PWH (mean increase 93.7% at 48 weeks).

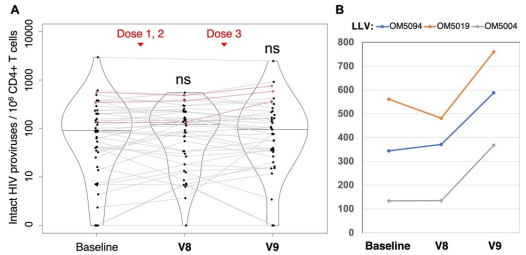

Fig. 5. Changes in the size of intact HIV reservoir (IPDA) in 45 PWH at 24 and 48 weeks post-D1 relative to the baseline (A). Changes in PWH with low-level viremia alone (B).

CONCLUSIONS

- PWH ≥ 55 y.o. show diminished nAb responses to SARS-CoV-2 with 2 vaccine doses which are 'rescued' after D3.
- They have lower than HIV⁻ anti-Spike IgA in saliva after vaccination which may affect protection (not shown).
- Enhanced anti-Spike T cell immunity in non-INR PWH suggests Th1 imprinting from pre-existing HIV infection.
- COVID-19 vaccines did not destabilize HIV reservoirs in most PWH but were associated with increased viral blips, and may pose potential risk in unsuppressed viremia.

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