

Dettaglio abstract

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Title: SARS-CoV-2 mRNA vaccination and viro-immunological changes in PLWH

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Vaccine in frail patients

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Abstract

Background: Despite anecdotal reports describing a transient increase in HIVRNA viral load (VL) and decrease of CD4 count after SARS-CoV-2 mRNA vaccination in people living with HIV (PLWH), whether vaccination has an impact on viro-immunological parameters remains to be investigated.

Methods: PLWH of the VAXICONA-ORCHESTRA cohort who received ≥ 1 dose of SARS-CoV-2 mRNA vaccine and for whom paired measures of immuno-virological markers [VL, CD4, CD8 count 1 month before and after the dose] were available, were included, stratified according to the time elapsed from ART initiation: less than 6 months (L6m) vs. more than 6 months (M6m). Paired t-test was used to verify whether a change in CD4, CD8 count (natural scale) or VL (log₁₀ scale) occurred over + 1 month around vaccine dose (VD). Subgroup analyses were performed according to i) VL and CD4 count 1 month before vaccination, ii) time of ART initiation. In addition, we conducted a sensitivity analysis restricted to participants with no evidence of natural infections at any time during the follow-up (established by anti-N+ result or recorded clinical evidence).

Results: N=473 PLWH were included, contributing 684 marker pairs: N=176 (26%) started ART L6m and 508 (74%) M6m; 17% were female, median age 55 y(IQR 46-60), CD4 count before VD was 480 cells/mm³ (286,711), CD8 790 (597,1103), 90% of participants had VL<50 cps/mL, 42% had ≥ 1 comorbidity, time since HIV diagnosis 9 years (4-18), 17% and 83% received 2 and 3 VDs, respectively. Pooling together all the VDs, over a median of 28 days (3-53) between pre- and post-VD value, CD4 count significantly increased by a mean of +18 cells/mm³ (SD 124; p<.001), CD8 by +13 (SD 360; p=0.345). VL decreased by -0.10 Log₁₀ (0.87; p=0.002), among PLWH with VL<50cps/mL pre-VD only 2% had VL>50 cps/mL and in 35% of those with VL >50 cps/mL pre-VD post-VD VL became ≤ 50 copies/mL. Similar results were observed when the analysis was restricted to those with VL ≤ 50 cps/mL pre-VD and to those with CD4 count ≤ 200 /mm³ (Tab. 1A). In this latter analysis we observed larger changes, possibly due to the regression to the mean. Results were also similar among participants who started ART M6m, thus minimizing the potential confounding effect of ART (Tab.1B) and after excluding those with evidence of natural infection at any time in follow-up (Tab.1C).

Discussion: Contrary to previous observations in PLWH, SARS-CoV-2 mRNA vaccination was not associated neither with a CD4 drop nor with transient increases in HIVRNA. If anything, a significant increase in CD4 count and a drop in HIV-RNA were observed, although the magnitude of the changes were of negligible clinical significance. In addition, there was no evidence of any effect on CD8 count.

Our findings are consistent with the hypothesis that SARS-CoV-2 mRNA vaccine is able to rapidly prime CD4 T spike specific cells independently from ART also in immuno-suppressed participants, emphasizing the usefulness of vaccination in advanced PLWH.

Table 1. Mean delta changes of paired viro-immunological markers \pm 1 month before and after each vaccine dose: A) All study participants; b) Participants with start of ART M6m; c) only vaccinated participants (with no previous natural SARS-CoV-2 infection) according HIVRNA and CD4 count at the time of vaccination

A				B				C			
Variable	N	Mean	SD	Variable	N	Mean	SD	Variable	N	Mean	SD
<i>All pairs</i>				<i>All pairs</i>				<i>All pairs</i>			
CD4 count, cells/mm ³	684	18.6	124.8	CD4 count, cells/mm ³	508	16.8	129.7	CD4 count, cells/mm ³	646	16.6	125.7
CD8 count, cells/mm ³	682	13.0	360.6	CD8 count, cells/mm ³	506	2.8	371.1	CD8 count, cells/mm ³	644	11.6	368.7
HIVRNA, cps/mL	675	-0.10	0.87	HIVRNA, cps/mL	500	-0.05	0.79	HIVRNA, cps/mL	638	-0.11	0.89
<i>Pairs with HIV RNA \leq50cps/mL at the time of vaccination</i>				<i>Pairs with HIV RNA \leq50cps/mL at the time of vaccination</i>				<i>Pairs with HIV RNA \leq50cps/mL at the time of vaccination</i>			
CD4 count, cells/mm ³	609	18.8	127.7	CD4 count, cells/mm ³	471	18.4	132.1	CD4 count, cells/mm ³	576	17.2	128.9
CD8 count, cells/mm ³	607	10.7	364.2	CD8 count, cells/mm ³	469	4.7	378.6	CD8 count, cells/mm ³	574	10.0	372.1
HIVRNA, cps/mL	607	-0.01	0.77	HIVRNA, cps/mL	469	-0.00	0.74	HIVRNA, cps/mL	574	-0.02	0.78
<i>Pairs with CD4 count \leq 200/mm³ at the time of vaccination</i>				<i>Pairs with CD4 count \leq 200/mm³ at the time of vaccination</i>				<i>Pairs with CD4 count \leq 200/mm³ at the time of vaccination</i>			
CD4 count, cells/mm ³	98	23.9	57.8	CD4 count, cells/mm ³	53	22.1	72.5	CD4 count, cells/mm ³	94	24.1	58.8
CD8 count, cells/mm ³	98	35.9	204.1	CD8 count, cells/mm ³	53	17.7	198.1	CD8 count, cells/mm ³	94	36.2	207.1
HIVRNA, cps/mL	98	-0.37	1.05	HIVRNA, cps/mL	53	-0.36	1.03	HIVRNA, cps/mL	94	-0.38	1.07