Dettaglio abstract

Title: Poor humoral immunogenicity to SARS-CoV-2 vaccination in people living with HIV (PLWH) with low CD4 count

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Immunological efficacy of SARS-CoV-2 vaccine I

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Abstract

Background: Data on SARS-CoV-2 vaccine immunogenicity in PLWH are currently limited, mostly collected in persons with high CD4 count from randomized trials. Large population studies characterizing the immune response after vaccination by CD4 count are lacking. Aim of this analysis was to investigate real-world antibody response against SARS-CoV-2 spike protein elicited after primary vaccination according to CD4 count in a large cohort of PLWH.
Methods: We included PLWH of the VAXICONA-ORCHESTRA cohort who received SARS-CoV-2 vaccine and for whom anti-S serology was available. Serologic titres were standardized in BAU/mL. Participants were stratified by CD4 count pre-vaccination (T0) (LCD4=CD4 count <200 cell/mm3; ICD4=CD4 count 201-500 cell/mm3; HCD4=CD4 count >500 cell/mm3). Immune response was defined as having anti-S ≥7.1 BAU/mL for Abbott, ≥0.82 BAU/mL for Roche and ≥4.8 BAU/mL for DiaSorin, while low response was defined as ≤46 BAU/mL regardless of assay. ANOVA was used to compare titres (log2 scale); association between CD4 groups and risk of undetectable/low level anti-S was evaluated by means of logistic regression.
Results: 2,017 PLWH were included (LCD4=145; ICD4=539; HCD4=1333); median age 53 years (IQR 45-59), median time from HIV diagnosis 12 years (6-22), median CD4 nadir 200 cell/mm3 (64-363), 89% HIV-RNA <50 copies/mL, 25% with a previous AIDS diagnosis, 25% with ≥1 comorbidity (Table 1). The proportion with undetectable/low immune response after a median of 28 days (21-28) after 1st dose was 33.9/75.6% for LCD4, 9.5/58.6% for ICD4 and 4.9/44.7% for HCD4 (P<0.0001/P<0.0001). Odds ratios from fitting a logistic regression are reported in Table 2. At a median of 50 days (31-77) from 2nd dose, the proportion with undetectable/low response were 9.8/30.8% for LCD4, 1.8/9.0% for ICD4 and 0.9/7.2% for HCD4 (P<0.0001/P<0.0001) (Figure 1). The adjusted mean (SD) levels of anti-S were 6.7 (3.7) log2 BAU/mL for LCD4, 8.6 (2.5) for ICD4 and 8.9 (2.4) for HCD4 (Fisher test P<0.0001, Figure 2).
Conclusions: In this large real world population sample, humoral immunogenicity after primary cycle of SARS- CoV-2 vaccination was lacking or poorly elicited in a consistent proportion of PLWH with CD4 count

<200/mm3. Having a CD4 count >500 cell/mm3 as comparator, a significant higher risk of lack of response after 1st dose and lower average levels after 2nd dose were also observed in PLWH with CD4 count of 201-500/mm3. CD4 count was confirmed as a strong predictor of humoral response to SARS-CoV-2 vaccination in PLWH. These findings are useful to inform policy makers regarding the use of additional and booster doses in PLWH

Table 1. Descriptive characteristics of study population

Characteristics	CD4 count				
	LCD4 N= 145	ICD4 N= 539	HCD4 N= 1333	p-value*	Total N= 2017
Age, years, median (IQR)	55 (46, 60)	54 (46, 60)	52 (44, 59)	<.001	53 (45, 59)
>=1 comorbidity, n(%)	44 (30.3)	139 (25.8)	325 (24.4)	0.271	508 (25.2)
Nadir CD4 count, cells/mm3, median (IQR)	41 (16, 82)	107 (42, 226)	279 (127, 428)	<.001	200 (64, 363)
Time from HIV diagnosis, years, median (IQR)	7 (1, 23)	10 (4, 23)	13 (7, 22)	<.001	12 (6, 22)
AIDS, n(%)	43 (29.7)	174 (32.9)	273 (21.0)	<.001	490 (24.8)
VL<=50 at T0, n(%)	64 (51.6)	347 (85.5)	1085 (94.9)	<.001	1496 (89.4)
Time between entry and response to 1st dose, days, median (IQR)	27 (21, 28)	28 (21, 28)	27 (21, 28)	0.519	28 (21, 28)
Time between entry and response to 2nd dose, days, median (IQR)	59 (51, 91)	65 (58, 91)	76 (59, 96)	<.001	70 (58, 92)
Time between 2nd dose and response to 2nd dose, days, median (IQR)	31 (30, 63)	49 (30, 71)	55 (31, 82)	<.001	50 (31, 77)

*Chi-square or Kruskal-Wallis test as appropriate; abbreviations: LCD4, CD4<200/mm³,ICD4, CD4 201-500/mm³, HCD4, CD4>500/mm³

Figure 1. Proportions of undetectable and low immune response by CD4 count and according to time evaluation (after the 1st and 2nd dose)
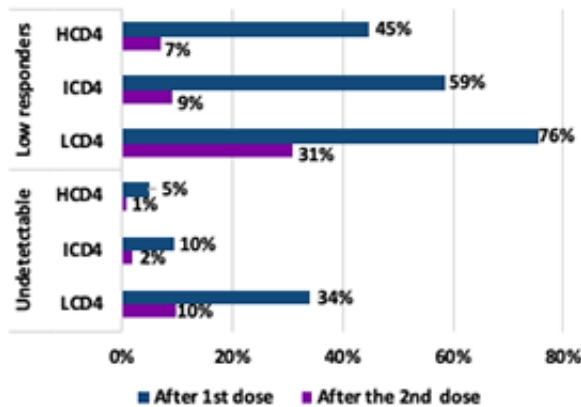

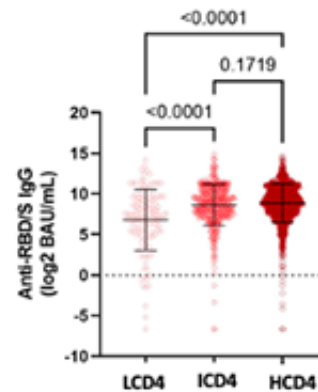### Figure 2. Anti-Spike IgG mean titres after the 2nd dose according to CD4 count

Table 2. OR of non-response to 1st dose and after 2nd dose from fitting a logistic regression analysis.

	Logistic regression of the probability of anti-S response post vaccination				
	Unadjusted		Adjusted*		
	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value	&Type III p-value
CD4 count	Undetectable - first dose				
HCD4	1		1		<.001
ICD4	2.06 (1.33, 3.20)	0.001	2.71 (1.47, 5.02)	0.001	
LCD4	10.00 (6.14, 16.26)	<.001	7.35 (3.60, 15.00)	<.001	
	Low level (below 46 BAU/mL) - first dose				
HCD4	1		1		<.001
ICD4	1.75 (1.39, 2.21)	<.001	2.36 (1.73, 3.23)	<.001	
LCD4	3.85 (2.46, 6.00)	<.001	4.39 (2.50, 7.70)	<.001	
	Undetectable - full cycle				
HCD4	1		1		<.001
ICD4	1.88 (0.79, 4.48)	0.157	1.87 (0.69, 5.10)	0.221	
LCD4	11.04 (4.93, 24.74)	<.001	7.95 (2.85, 22.19)	<.001	
	Low level (below 46 BAU/mL) - full cycle				
HCD4	1		1		<.001
ICD4	1.28 (0.88, 1.86)	0.198	1.15 (0.75, 1.76)	0.528	
LCD4	5.74 (3.75, 8.79)	<.001	4.00 (2.39, 6.70)	<.001	

*adjusted for age, CD4 nadir,VL<=50 copies/mL at T0 and no. of comorbidities
&from the adjusted model; abbreviations: LCD4, CD4<200/mm³,ICD4m CD4 201-500/mm³, HCD4, CD4>500/mm³