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

12. COVID-19

12g. Vaccine development, trials, efficacy, policy

A. Antinori¹, A. Cozzi-Lepri², A. Vergori¹, A. Tavelli³, L. Marconi⁴, S. Cicalini¹, A.M. Azzini⁵, A. Sartor⁶, A. Rodano⁷, S. Meschi¹, C. Agrati¹, F.M. Fusco⁸, E. Righi⁵, F. Abbruzzani⁴, G. Marchetti⁷, E. Girardi¹, P. Viale⁴, M. Giannella⁴, E. Tacconelli⁵, A. D'Arminio Monforte³.¹National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS - Rome (Italy), ²CREME, Institute for Global Health, UCL - London (United Kingdom), ³ASST Santi Paolo e Carlo, University of Milan - Milano (Italy), ⁴Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna - Bologna (Italy), ⁵Division of Infectious Diseases, Department of Diagnostics and Public Health, University of Verona - Verona (Italy), ⁶Microbiology Unit, Udine University Hospital - Udine (Italy), ⁷ASST Santi Paolo e Carlo, University of Milan - Milan (Italy), ⁸AORN Ospedali dei Colli, Cotugno Hospital - Naples (Italy)**Please add any third party affiliations (research group, study group etc.) for your 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. Aim of this analysis was to investigate the association between CD4 count and anti-S response after primary vaccination in a real-world setting.

Methods

We included PLWH of the VAXICONA-ORCHESTRA cohort who received SARS CoV2 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

1,229 PLWH were included (LCD4=111; ICD4=372; HCD4=746); median age 53 yrs (IQR 45-59), median time from HIV diagnosis 12 yrs (6-24), median CD4 nadir 179 cell/mm³ (55-343), 89% HIV-RNA <50 copies/mL, 24% with a previous AIDS diagnosis, 27% with ≥ 1 comorbidity. The proportion with undetectable/low immune response after 1st dose was 37.4/79.1% for LCD4, 9.3/58.7% for ICD4 and 4.3/46.2% for HCD4 (P<0.0001/P<0.0001). Odds ratios from fitting a logistic regression are reported in Table 1. After a median of 35 days (30-63) from 2nd dose, the proportion with undetectable/low response were 11.7/32.4% for LCD4, 1.6/8.6% for ICD4 and 0.7/5.8% for HCD4 (P<0.0001/P<0.0001). The adjusted mean (SD) levels of anti-S were 6.6 (4.0) log₂ BAU/mL for LCD4, 8.7 (2.6) for ICD4 and 9.2 (2.3) for HCD4 (Fisher test P<0.0001, Figure 1).

Conclusions

Humoral immunogenicity after primary SARS CoV2 vaccination was lacking or poorly elicited in a substantial proportion of PLWH with CD4 count <200/mm³. Having >500 as the comparator, a significantly higher risk of lack of response after 1st dose and lower average levels after 2nd dose was also observed in PLWH with CD4 count of 201-500/mm³. A third additional dose is mandatory in PLWH with CD4 <200/mm³ and should be considered in those with CD4 between 200-500 cell/mm³.

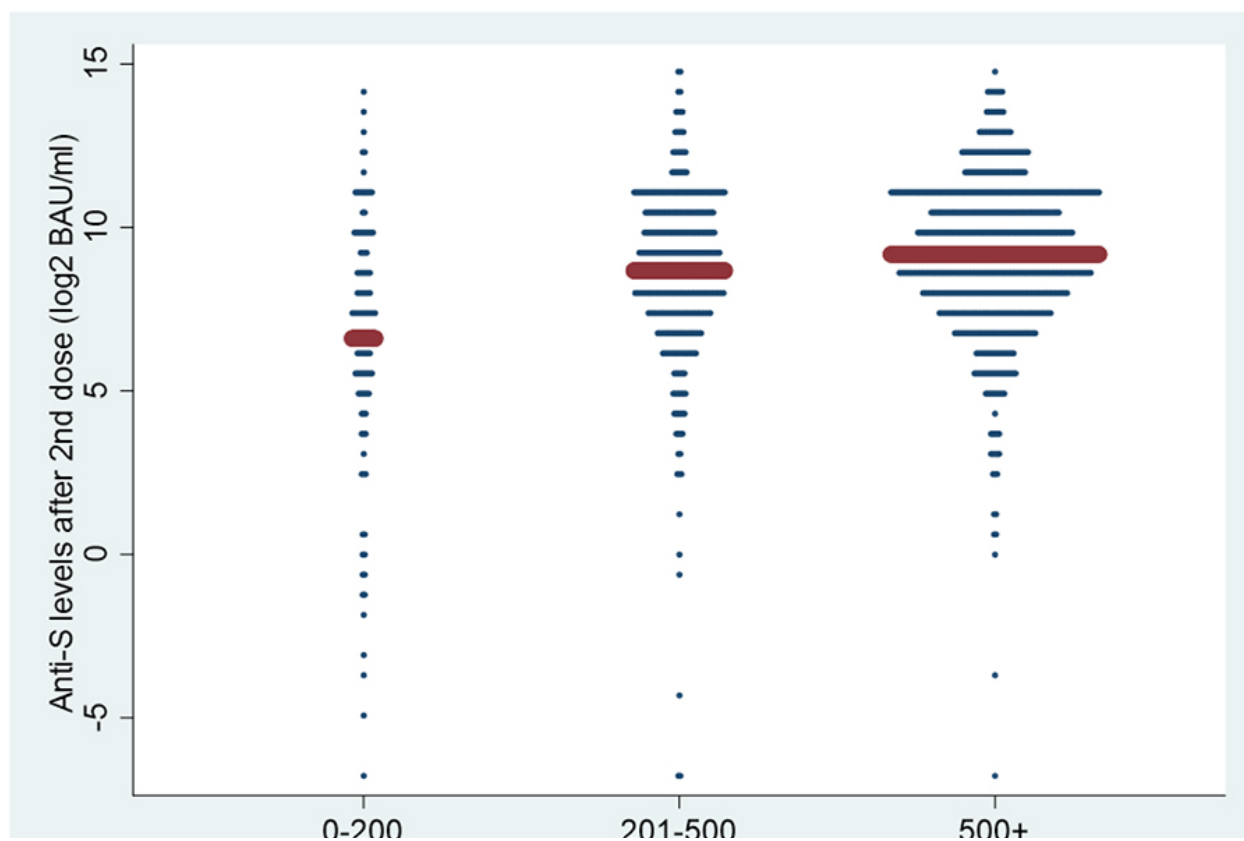
Table 1. Odds ratios of having undetectable/low level of anti-S response after priming dose and after full cycle of vaccination from fitting a logistic regression analysis. OR=odds ratio; AOR=adjusted odds ratio. All models were controlled for age, CD4 nadir, HIV-RNA at T0 and number of concomitant co-morbidities.

Logistic regression of the probability of anti-S response post vaccination

	Unadjusted		Adjusted*		&Type III p-value
	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value	
CD4 count					
	Undetectable - first dose				
500+	1		1		<.001
201-500	2.27 (1.32, 3.91)	0.003	2.61 (1.32, 5.15)	0.006	
0-200	13.17 (7.38, 23.49)	<.001	9.19 (4.23, 19.97)	<.001	
	Low level (below 46 BAU/mL) - first dose				
500+	1		1		<.001
201-500	1.66 (1.26, 2.18)	<.001	1.90 (1.35, 2.69)	<.001	
0-200	4.42 (2.60, 7.51)	<.001	4.35 (2.21, 8.58)	<.001	
	Undetectable - full cycle				
500+	1		1		<.001
201-500	2.43 (0.74, 8.01)	0.145	2.37 (0.71, 7.89)	0.161	
0-200	19.66 (6.86, 56.33)	<.001	11.64 (3.55, 38.15)	<.001	
	Low level (below 46 BAU/mL) - full cycle				
500+	1		1		<.001
201-500	1.54 (0.96, 2.48)	0.076	1.47 (0.88, 2.45)	0.143	
0-200	7.85 (4.75, 12.97)	<.001	5.24 (2.88, 9.55)	<.001	

*adjusted for age, CD4 nadir, VL<=50 copies/mL at T0 and no. of comorbidities
&from the adjusted model

Figure 1. Magnitude of anti-S response (\log_2 BAU/mL) after second dose of SARS-CoV-2 vaccine according to CD4 count at the time of priming dose. Data are expressed as geometric mean titres (line orange) and SD (line green and red). P value at Fisher test <0.0001; P value after Dunn-Bonferroni correction for multiple comparisons: CD4 \leq 200 vs CD4 201-500 P<0.0001; CD4 \leq 200 vs CD4 >500 P<0.0001; CD4 201-500 vs CD4 >500 P=0.0028.



CD4 count at T0

Keyword 1

PLWH

Keyword 2

COVID-19 Vaccination response

Keyword 3

imunological response

Conflicts of interest

Do you have any conflicts of interest to declare?

I have no potential conflict of interest to report