

Dettaglio abstract

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Title: Humoral immunogenicity to SARS-CoV-2 mRNA vaccine third additional/booster shot in people living with HIV (PLWH) by current CD4 count

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Immunological efficacy of SARS-CoV-2 vaccine I

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Abstract

Background: In Italy, from September 2021, administration of a 3rd additional/booster dose (3D) of SARS-CoV-2 vaccine was approved for PLWH with advanced disease. Observational data on immunogenicity after a 3D in PLWH are currently limited. Aim was to investigate real-world antibody response against SARS-CoV-2 spike protein elicited after a 3D of mRNA vaccination, according to CD4 count, in a large cohort of PLWH.

Methods: We included PLWH of the VAXICONA-ORCHESTRA cohort who previously received a primary cycle of SARS-CoV-2 mRNA vaccine, who were infused with a mRNA 3D 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 ANOVA and logistic regression.

Results: 625 PLWH included (LCD4=96; ICD4=199; HCD4=330); median age 56 years (IQR 48-61), median time from HIV diagnosis 11 years (5-23), median CD4 nadir 124 cell/mm³ (39-299), 89% HIV-RNA <50 copies/mL, 30% with a previous AIDS diagnosis, 39% with ≥ 1 comorbidity. PLWH received the 3D at a median of 164 days (151-173) from the second dose (Table 1). The proportion with undetectable/low response after a median of 31 days (30-62) after the 2nd dose was originally 12.5/38.9% for LCD4, 1.4/10.9% for ICD4 and 0.9/12.2% for HCD4 ($P < 0.0001/P < 0.0001$). After a median of 164 days (151-193) from the 2nd dose the same proportion increased to 15.6/72.7% for LCD4, 5.6/33.9% for ICD4 and 8.8/27.5% for HCD4 ($P < 0.0001/P < 0.0001$). After at a median of 29 days (16-56) after the 3D, the proportion of PLWH with undetectable/low immune response showed a sharp decline to 5.21/12.5% for LCD4, 0.5/2.0% for ICD4 and 0.3/1.2% for HCD4 ($P < 0.0001/P < 0.0001$). Odds ratios from fitting a logistic regression for the 3D are reported in Table 2. The adjusted mean (SD) levels of anti-S after 2nd dose were 3.4 (3.4) log₂ BAU/mL for LCD4, 5.9 (3.2) for ICD4 and 6.1 (3.3) for HCD4, (Fisher test $P < 0.0001$, Figure 1a) and 8.7 (3.4) log₂ BAU/mL for LCD4, 10.6 (2.0) for ICD4 and 11.1 (2.2) for HCD4, after 3D (Fisher test $P < 0.0001$, Figure 1b).

Conclusions: In PLWH, a 3D of SARS-CoV-2 mRNA vaccine, elicited a strong humoral immune response,

higher than observed after the primary vaccination, even in patients with poor CD4 count. The 3D quickly over-compensated the waning of immune response already seen a few months after the 2nd dose. A CD4 count <200 cell/mm³ was independently associated with a 3-fold higher risk of low antibody response after 3D vs. >500 cell/mm³. These data are essential for targeted strategies for appropriate delivery of a 4th dose in PLWH.

Table 1. Descriptive characteristics of study population

Characteristics	CD4 count			p-value*	Total N= 625
	LCD4 N= 96	ICD4 N= 199	HCD4 N= 330		
Age, years, median (IQR)	57 (48, 61)	56 (49, 63)	55 (47, 61)	0.152	56 (48, 61)
>=1 comorbidity, n(%)	31 (32.3)	79 (39.7)	133 (40.3)	0.352	243 (38.9)
Nadir CD4 count, cells/mm ³ , median (IQR)	41 (15, 80)	64 (23, 161)	250 (96, 410)	<.001	124 (39, 299)
Time from HIV diagnosis, years, median (IQR)	8 (1, 24)	9 (4, 22)	12 (8, 24)	<.001	11 (5, 23)
AIDS, n(%)	24 (25.0)	75 (37.7)	89 (27.0)	0.017	188 (30.1)
VL<=50 at T0, n(%)	43 (52.4)	146 (93.6)	279 (97.6)	<.001	468 (89.3)
Times (days), medians (IQR)					
From 2nd dose to response	31 (30, 32)	31 (30, 56)	35 (30, 67)	<.001	31 (30, 62)
From 2nd dose to 3rd dose	154 (137, 160)	159 (140, 193)	175 (160, 196)	<.001	164 (151, 193)
From 3rd dose to response	18 (15, 28)	29 (16, 58)	36 (17, 58)	<.001	29 (16, 56)

*Chi-square or Kruskal-Wallis test as appropriate; abbreviations: LCD4, CD4<200/mm³, ICD4m 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 2nd, at waning post 2nd and after the 3rd dose)

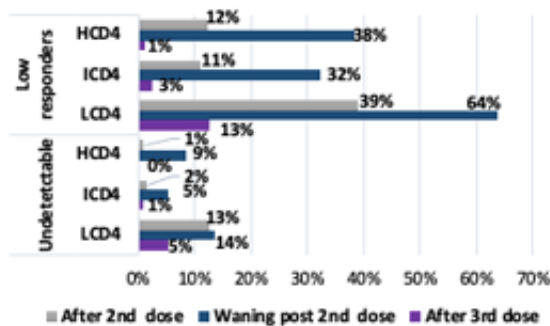


Figure 2. Anti-Spike IgG mean titres A) after the 2nd dose and after the 3rd, according to CD4 count.

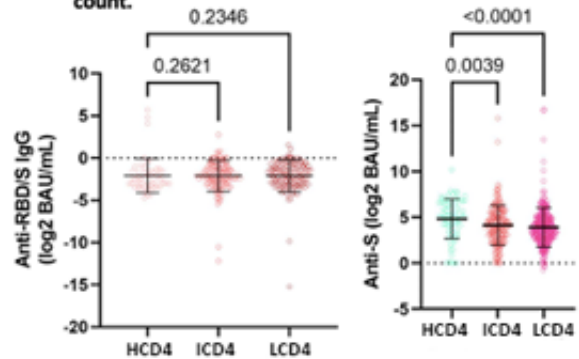


Table 2. OR of non-response to 2nd dose, after waning of 2nd dose and after 3rd dose from fitting a logistic regression analysis.

CD4 count	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	
Undetectable – after 2 nd dose					
HCD4	1		1		0.005
ICD4	1.46 (0.20, 10.45)	0.709	1.55 (0.21, 11.25)	0.666	
LCD4	15.07 (3.17, 71.56)	<.001	11.36 (2.08, 61.88)	0.005	
Low level (below 46 BAU/mL) – after 2 nd dose					
HCD4	1		1		<.001
ICD4	0.88 (0.45, 1.70)	0.701	0.84 (0.41, 1.71)	0.627	
LCD4	4.58 (2.45, 8.57)	<.001	3.82 (1.78, 8.19)	<.001	
Undetectable - waning of 2 nd dose					
HCD4	1		1		0.201
ICD4	0.62 (0.29, 1.34)	0.226	0.67 (0.31, 1.46)	0.313	
LCD4	1.92 (0.91, 4.06)	0.089	1.64 (0.67, 4.00)	0.276	
Low level (below 46 BAU/mL) - waning of 2 nd dose					
HCD4	1		1		<.001
ICD4	1.35 (0.90, 2.04)	0.151	1.56 (1.00, 2.44)	0.050	
LCD4	7.04 (3.98, 12.45)	<.001	4.32 (2.23, 8.36)	<.001	
Undetectable - after 3 rd dose					
HCD4	1		1		0.451
ICD4	1.83 (0.11, 29.41)	0.671	1.53 (0.09, 25.78)	0.767	
LCD4	18.51 (2.13, 160.8)	0.008	4.41 (0.33, 59.31)	0.264	
Low level (below 46 BAU/mL) - after 3 rd dose					
HCD4	1		1		0.005
ICD4	0.99 (0.48, 2.06)	0.985	0.95 (0.45, 1.99)	0.893	
LCD4	4.40 (2.29, 8.46)	<.001	3.43 (1.58, 7.44)	0.002	

*adjusted for age, CD4 nadir, VL<=50 copies/mL at T0 and no. of comorbidities;
†from the adjusted model; abbreviations: LCD4, CD4<200/mm³, ICD4, CD4 201-500/mm³, HCD4, CD4>500/mm³