Reduced T-cell response following a third dose of SARS-CoV-2 vaccine in infection-naïve people living with HIV

Breach Symposium

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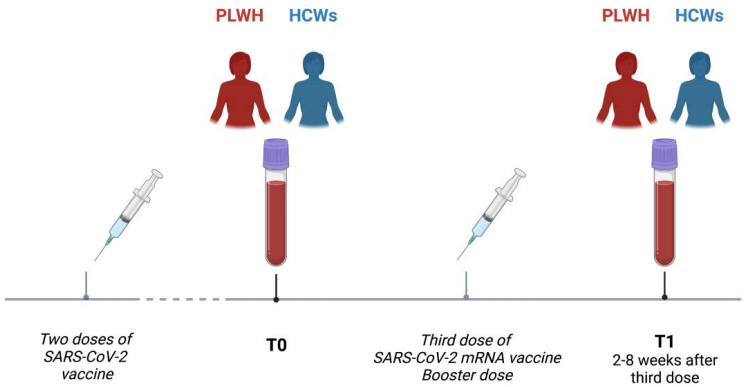
Objectives

1. Characterise **humoral and T-cell immune responses** against SARS-CoV-2 before and after administration of the third dose of vaccine and compared these responses with those of HIV-negative control individuals

2. Identify factors associated with poorer responses

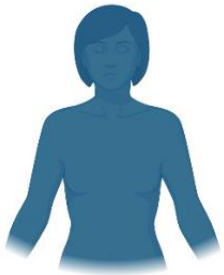
3. Investigate the impact of previous SARS-CoV-2 infections on immune responses



Methods: Populations

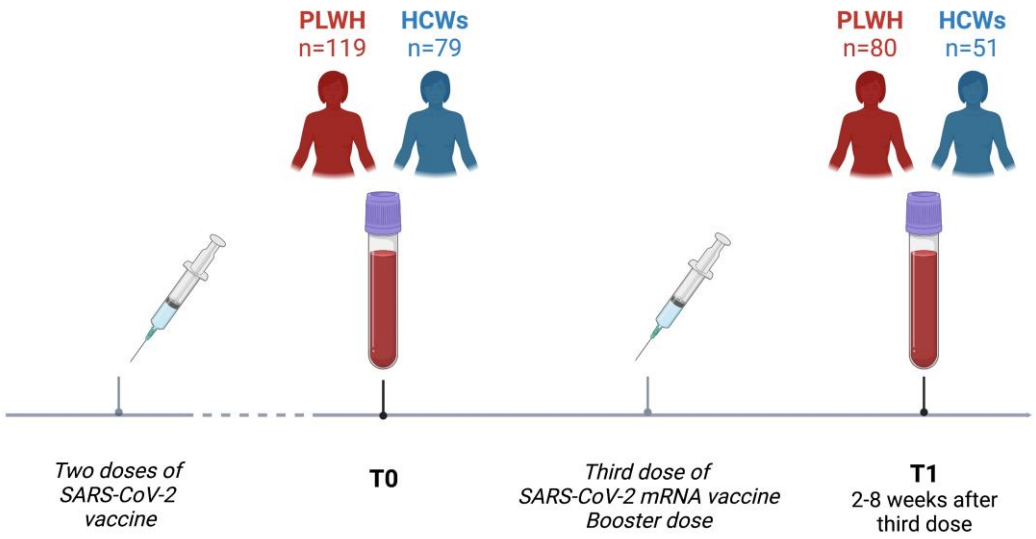
PLWH

HCWs



- ≥ 18 years of age
- Two-doses regimen of SARS-CoV-2 vaccination, either BNT162b2, mRNA-1273 or ChAdOx1-S

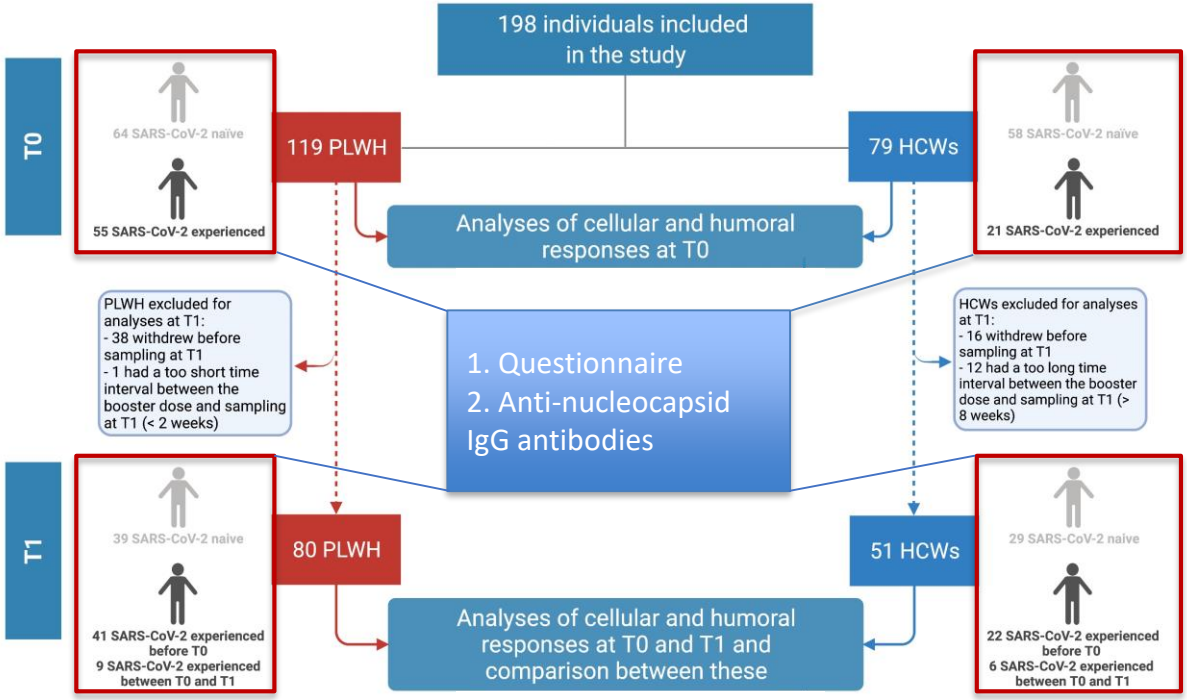
Methods: Populations



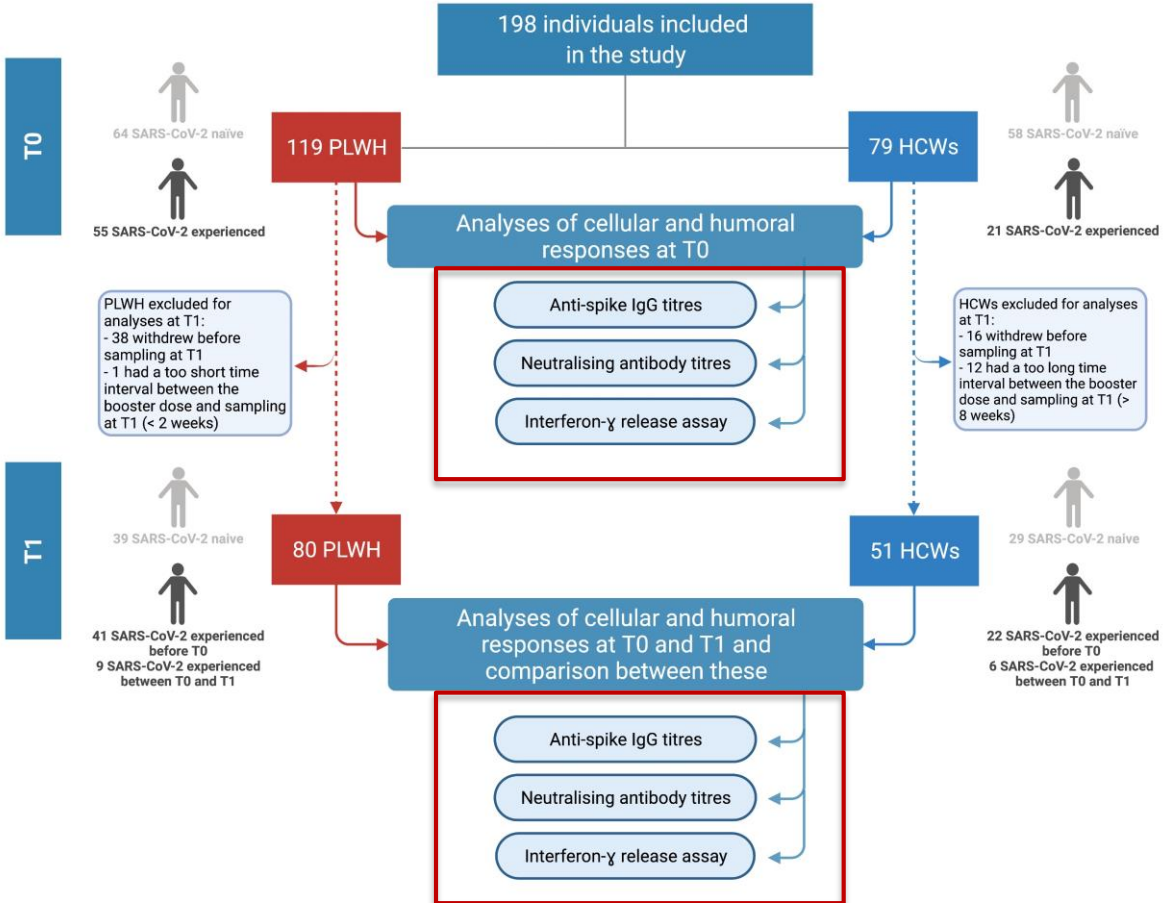
- The third dose, either BNT162b2 or mRNA-1273, was administered through Belgium's vaccination campaign

- Peripheral blood was sampled before the third dose (T0) and two to eight weeks after the third dose of vaccine (T1)

Study Design



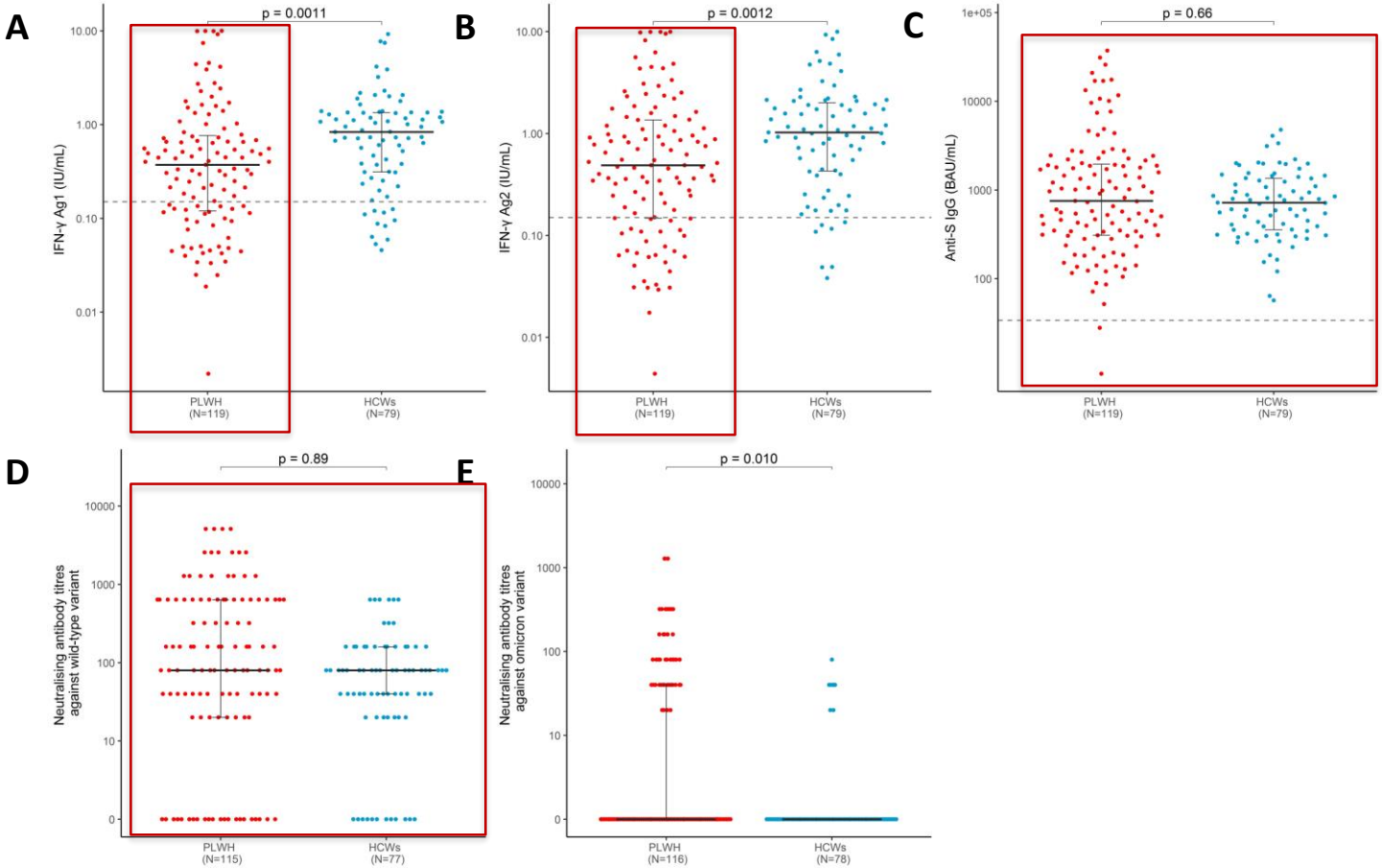
Study Design



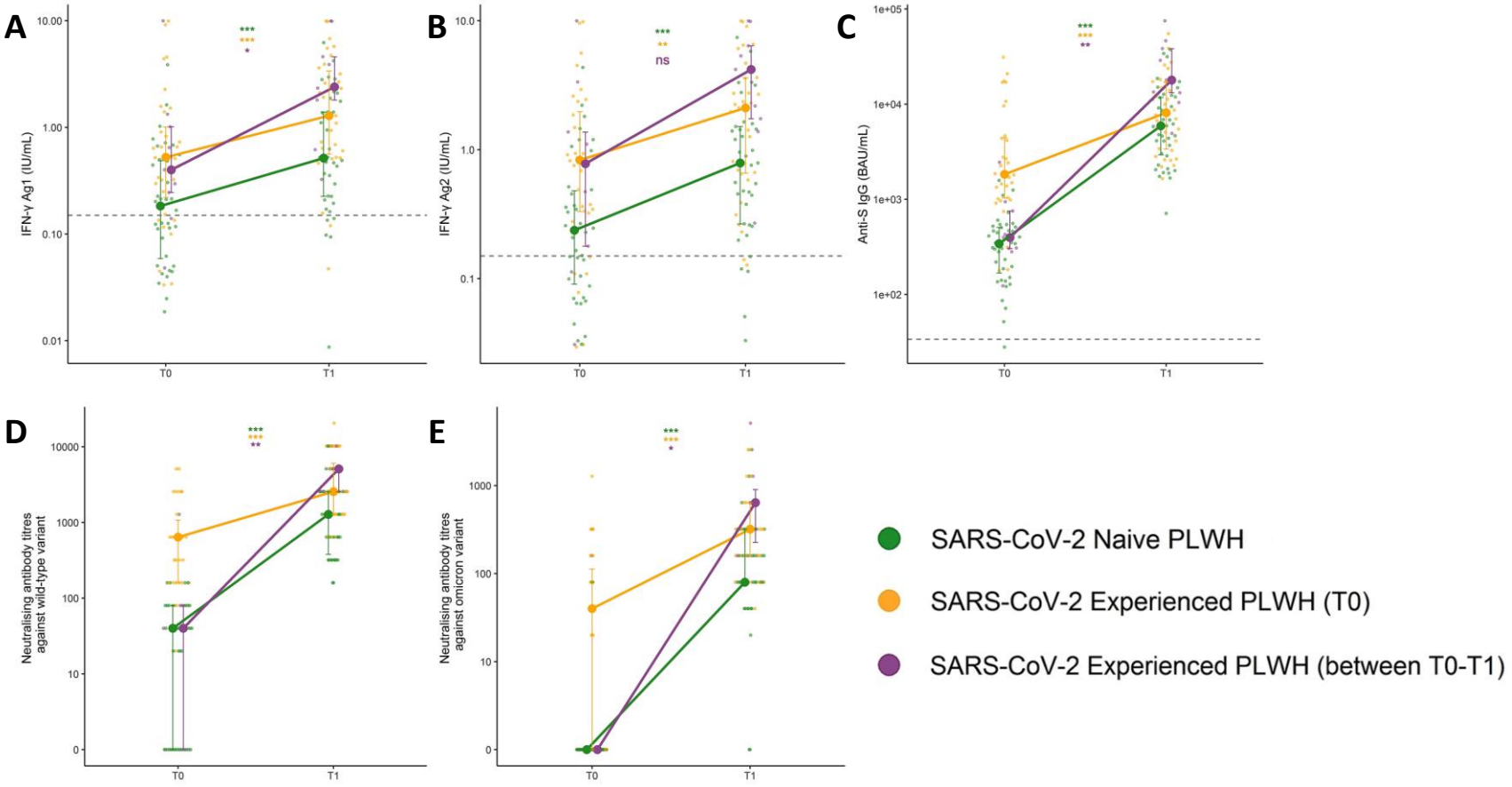
Background Characteristics of PLWH at T0 and T1

Variable	PLWH at T0 (n=119)	PLWH at T1 (n=80)
HIV infection		
HIV-1	118 (99.2)	79 (98.8)
HIV-2	1 (0.8)	1 (1.2)
Prior AIDS diagnosis	45 (37.8)	27 (33.8)
Time at T0 since HIV diagnosis (years)	11 (6-18)	11 (6.5-18)
<1	1 (0.8)	1 (1.2)
1-5	27 (22.7)	17 (21.3)
6-10	26 (21.9)	17 (21.3)
>10	65 (54.6)	45 (56.2)
Nadir CD4+T cell count per µL	259 (163-462)	292 (166-502)
<200	39 (32.8)	25 (31.2)
≥200	80 (67.2)	55 (68.8)
Last CD4+T cell count per µL (2021 or 2022)	680 (546-898)	743 (592-940)
<350	8 (6.7)	3 (3.7)
350-499	17 (14.3)	11 (13.8)
≥500	94 (79.0)	66 (82.5)
CD4/CD8 ratio, n=117	1.03 ± 0.57	1.1 ± 0.57
<0.6	25 (21.4)	16 (20.0)
0.6-1	40 (34.2)	26 (32.5)
>1	52 (44.4)	38 (47.5)
~~Last plasma viral load copies/mL~~	~~<20 (<20-<20)~~	~~<20 (<20-<20)~~
~~<50~~	~~112 (94.1)~~	~~75 (93.8)~~
Time on ART (years)	10.7 ± 6.6	10.7 ± 6.9

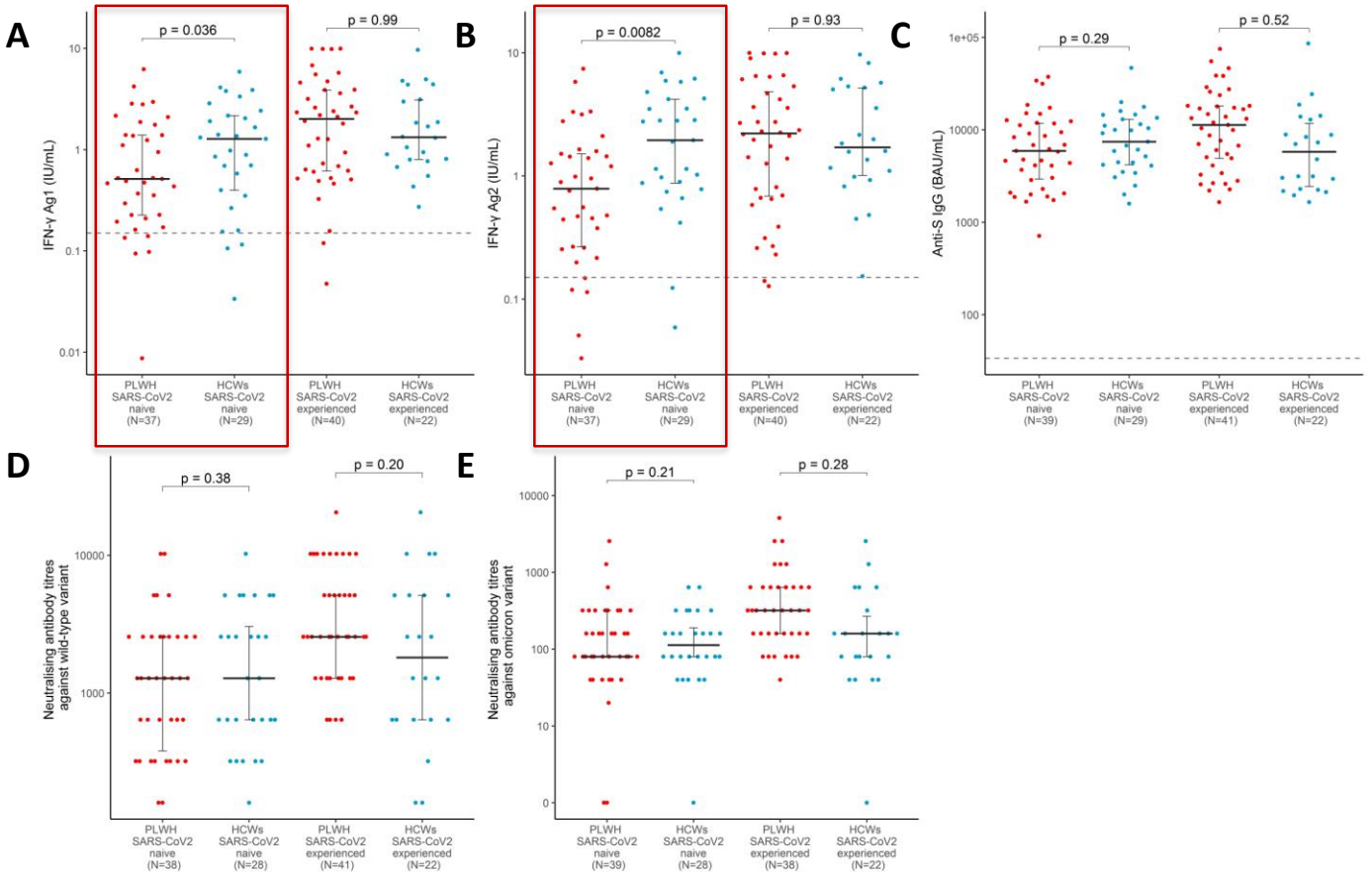
Results: Before The Third Dose (T0)



Results: Evolution T0-T1 Among PLWH



Results: After The Third Dose (T1)



Conclusion

- PLWH show similar humoral immune responses following the third dose of SARS-CoV-2 vaccine compared to HIV-negative individuals

- PLWH with no prior SARS-CoV-2 infection show reduced T-cell response following the third dose of SARS-CoV-2 vaccine compared to HIV-negative individuals

- Hybrid immunity induces similar T-cell responses between PLWH and HIV-negative individuals

Poster

Reduced T-cell response following a third dose of SARS-CoV-2 vaccine in infection-naïve people living with HIV

Majdouline El Moussaoui, Salomé Desmecht, Aleksandr Tashkeev, Nicolas Lambert, Nathalie Maes, Joachim Braghini, Nicole Marechal, Céline Quintana, Karine Briquet, Stéphanie Goffiot, Françoise Toussaint, Marie-Pierre Hayette, Pieter Vermeersch, Laurence Lutteri, Céline Grégoire, Yves Beguin, Souad Rahmouni, Michel Moutschen, Daniel Desmecht, Gilles Darcis

BACKGROUND

Two doses of SARS-CoV-2 mRNA-based vaccines were shown to elicit strong humoral and cellular immune responses in the general population and are effective for the prevention of severe forms of COVID-19 and related hospitalisations and deaths [1]. However, both immunity waning and emergence of variants escaping vaccine-induced immune response, justified the implementation of a third dose of vaccine, sometimes referred to as «booster» [2]. The latter effectively yields a potent cross-neutralising response against SARS-CoV-2 Omicron variant in the general population [3]. Although encouraging, if such statement can be generalised to specific immunocompromised populations is still unknown. People living with HIV (PLWH) were poorly represented in large-scale vaccine clinical trials, thereby preventing investigators to provide a clear-cut answer about the clinical efficacity of those vaccines in this specific population. Therefore, there is a pressing need to better understand the impact of vaccination against SARS-CoV-2, including administration of a third "booster" dose, on cellular and humoral immune responses of PLWH.

METHODS

We prospectively evaluated humoral and T-cell immune responses before (T0) and after (T1) administration of a third dose of SARS-CoV-2 vaccine, either BNT162b2 or mRNA-1273, in PLWH followed-up at the University Hospital of Liège (Belgium) and compared these with those of HIV-negative healthcare workers (HCWs). Biological analyses at each sampling timepoint included quantification of anti-trimeric spike protein specific IgG (anti-S IgG), 50% neutralising antibody titres against wild-type (WT) and Omicron (BA.1/B.1.1.529) strains, and SARS-CoV-2-specific interferon-gamma (IFN-γ) release using the QuantiFERON SARS-CoV-2 assay which contains two different pools (Ag1 and Ag2) of spike-embedded peptides.

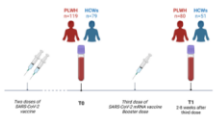


Fig. 1

RESULTS

119 PLWH and 79 HCWs were enrolled in the study and constituted the study cohort for analysis at T0. Among them, 80 PLWH and 51 HCWs completed the whole study and constituted the study cohort for T1 (Fig1). 84% PLWH and all HCWs received BNT162b2 as first two doses of vaccine. For the third dose, all HCWs and 52.5% PLWH received BNT162b2 and the remaining 47.5% received mRNA-1273. All PLWH except one were infected with HIV-1, with a median time since diagnosis of 11 years. All were on antiretroviral therapy. Among PLWH who fulfilled the whole study, median $CD4^+$ T cell count was 743/µL (IQR 592-940) and 5 patients had a viral load over 50 copies/mL. Before the third vaccine dose (T0), SARS-Cov-2 specific IFN-γ production was significantly lower in PLWH than in HCWs ($p<0.01$). In contrast, neutralising antibody titres (nAbTs) against Omicron were higher in PLWH ($p=0.01$). Anti-S IgG levels and nAbTs against WT were similar between the two groups. Considering participants' history of SARS-CoV-2 infection, IFN-γ production was lower only among SARS-CoV-2 naïve PLWH ($p<0.01$). Administration of a third dose of the SARS-CoV-2 vaccine elicited a significant increase in every parameter reflecting immune response among both HCWs and PLWH ($p<0.001$). Evolution between T0 and T1 of any of the parameters was not significantly different between PLWH and HCWs. The proportion of PLWH with detectable Omicron nAbTs rose from 27.3% to 87.4% but median Omicron nAbTs remained 8-fold lower than median anti-WT titre ($p<0.001$). Furthermore, nAbTs against Omicron and WT were both significantly lower among SARS-CoV-2 naïve PLWH compared to those previously infected ($p<0.001$).

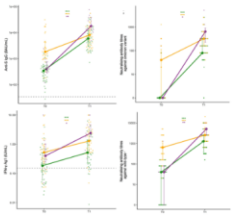


Fig. 2

After three doses of vaccine, we did not find a significant difference between PLWH and HCWs in any of the immune parameters investigated. However, considering participants' history of SARS-CoV-2 infection, IFN-γ production was still lower among SARS-CoV-2 naïve PLWH compared to naive HCWs ($p=0.036$ and $p=0.0082$ for Ag1 and Ag2, respectively), whereas it was similar between SARS-CoV-2 experienced PLWH and HCWs (Fig3). Subgroups analyses found no significant difference between immune responses of HIV-infected individuals according to their $CD4^+$ T cell count or $CD4^+/CD8^+$ T cell ratio.

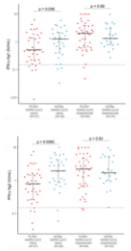


Fig. 3

CONCLUSION

Administration of a third dose of SARS-CoV-2 vaccine considerably enhanced SARS-CoV-2 specific humoral and T-cell immunity in PLWH. Humoral immune responses were similar between PLWH and HIV-negative individuals, both before and after the third dose. However, our data raise concerns about the vaccine's ability to induce protective T-cell immune response among PLWH with no history of SARS-CoV-2 infection. Further studies are needed to understand the clinical consequences of such observations and characterise the potential protective advantage of hybrid immunity in PLWH.

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Publication

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JOURNAL OF INFECTION

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Thank you for your attention!

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Background

- Clinical trials and real-world data have shown vaccination against SARS-CoV-2 to be highly effective against COVID-19 infection and severe outcomes
- Immunity waning and emergence of variants escaping vaccine-induced immune response, most notably the B.1.1.529 (Omicron) variant, justified the implementation of a third dose of mRNA vaccine, sometimes referred to as «booster»
- A booster dose vaccine has been recommended in Belgium for > years
- Real-world evidence on the effectiveness of booster dose vaccine in people living with HIV (PLWH) remains limited

Polack, et al., 2020, NEJM; Andrews, et al. 2022, Nature Medicine

Background characteristics of PLWH and HCWs at T0 and T1

Variable	PLWH at T0 (n=119)	HCWs at T0 (n=79)	p-value	PLWH at T1 (n=80)	HCWs at T1 (n=51)	p-value
Male sex	59 (49.6)	13 (16.5)	<0.0001	43 (53.8)	11 (21.6)	0.0003
Age (Years)	45.2 ± 10.6	43.7 ± 11.5	0.36	45.6 ± 10.7	43.0 ± 10.0	0.18
18-29	6 (5.0)	7 (8.9)		4 (5.0)	2 (3.9)	
30-39	36 (30.2)	27 (34.2)		24 (30.0)	22 (43.1)	
40-49	36 (30.2)	19 (24.0)		21 (26.2)	13 (25.5)	
50-59	29 (24.4)	17 (21.5)		22 (27.5)	10 (19.6)	
≥60	12 (10.1)	9 (11.4)		9 (11.3)	4 (7.8)	
BMI (kg/m²)	28.0 ± 5.1	25.1 ± 6.2, n=76	0.0006	27.5 ± 5.6	25.9 ± 6.9, n=50	0.13
Underweight (<18.5)	0 (0.0)	2 (2.6)		0 (0.0)	2 (4.0)	
Normal range (18.5-24.9)	34 (28.6)	38 (50.0)		29 (36.2)	22 (44.0)	
Overweight (25-29.9)	50 (42.0)	24 (31.6)		34 (42.5)	17 (34.0)	
Obese (≥30)	35 (29.4)	12 (15.8)		17 (21.3)	9 (18.0)	
Ethnicity			-			-
Caucasian	45 (37.8)	-		34 (42.5)	-	
African	69 (58.0)	-		41 (51.3)	-	
Other	5 (4.2)	-		5 (6.2)	-	
Medical history						
Diabetes mellitus	8 (6.7)	3 (3.8)	0.53	5 (6.2)	1 (2.0)	0.40
Hypertension	32 (26.9)	14 (17.7)	0.13	18 (22.5)	7 (13.7)	0.21
Heart failure coronary artery disease	2 (1.7)	1 (1.3)	-	2 (2.5)	0 (0.0)	-
Stroke	2 (1.7)	0 (0.0)	-	1 (1.2)	0 (0.0)	-
Liver disease	1 (0.8)	0 (0.0)	-	1 (1.2)	0 (0.0)	-
Kidney disease	0 (0.0)	0 (0.0)	-	0 (0.0)	0 (0.0)	-
Chronic lung disease	1 (0.8)	0 (0.0)	-	1 (1.2)	0 (0.0)	-
Asthma	0 (0.0)	6 (7.6)	0.0036	0 (0.0)	3 (5.9)	0.0028
Autoimmune disease	1 (0.8)	4 (5.1)	0.083	0 (0.0)	2 (3.9)	-
Hematological cancer	0 (0.0)	4 (5.1)	-	0 (0.0)	1 (2.0)	-
Non hematological cancer	9 (7.6)	4 (5.1)	0.74	7 (8.8)	4 (7.8)	1.0
Solid-organ/cell transplantation	0 (0.0)	0 (0.0)	-	0 (0.0)	0 (0.0)	-
Immunosuppressive drugs			-			-
Corticosteroids	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	
Other	1 (0.8)	1 (1.3)		0 (0.0)	0 (0.0)	

Background characteristics of PLWH and HCWs at T0 and T1

Variable	PLWH at T0 (n=119)	HCWs at T0 (n=79)	p-value	PLWH at T1 (n=80)	HCWs at T1 (n=51)	p-value
Previous SARS-CoV-2 infection (before T1)	-	-	-			
Questionnaire	-	-	-	15 (18.8)	18 (35.3)	0.033
Positive anti-N antibody	-	-	-	40 (50.0)	17 (34.0), n=50	0.074
SARS-CoV-2 experienced*	-	-	-	41 (51.2)	22 (43.1)	0.37
Experienced (between T0 and T1)	-	-	-	9 (11.2)	6 (11.7)	-
First vaccine dose			-			-
BNT162b2 mRNA (Pfizer)	101 (84.9)	79 (100.0)		69 (86.2)	51 (100.0)	
mRNA-1273 (Moderna)	8 (6.7)	0 (0.0)		4 (5.0)	0 (0.0)	
ChAdOx1-S (Astra Zeneca)	10 (8.4)	0 (0.0)		7 (8.8)	0 (0.0)	
Second vaccine dose			-			-
BNT162b2 mRNA (Pfizer)	100 (84.0)	79 (100.0)		69 (86.2)	51 (100.0)	
mRNA-1273 (Moderna)	9 (7.6)	0 (0.0)		4 (5.0)	0 (0.0)	
ChAdOx1-S (Astra Zeneca)	10 (8.4)	0 (0.0)		7 (8.8)	0 (0.0)	
Third vaccine dose			-			-
BNT162b2 mRNA (Pfizer)	-	-		42 (52.5)	51 (100.0)	
mRNA-1273 (Moderna)	-	-		38 (47.5)	0 (0.0)	
Time between first and second vaccine dose (weeks)	5.0 (4.0-5.0)	3.0 (3.0-3.1)	<0.0001	5.0 (4.4-5.0)	3.0 (3.0-3.1)	<0.0001
Time between second vaccine dose and sample at T0 (weeks)	25 (23-28)	24 (24-24)	0.025	25 (23-27)	24 (24-24)	0.014
Time between second and third vaccine dose (weeks)	-	-	-	27 (25-31)	38 (35-39)	<0.0001
Time between third vaccine dose and sample at T1 (weeks)	-	-	-	2.4 (3.1-3.9)	4.7 (4.0-8.0)	<0.0001
Time between T0 and T1 (weeks)	-	-	-	5 (4-6)	19 (18-19)	<0.0001

Results: Evolution T0-T1 among HCWs