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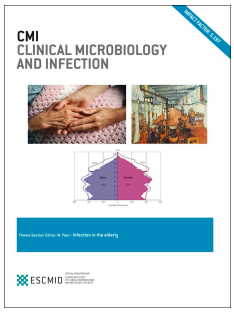

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PII: S1198-743X(21)00423-7

DOI: https://doi.org/10.1016/j.cmi.2021.07.031

Reference: CMI 2638

To appear in: *Clinical Microbiology and Infection*

Received Date: 26 May 2021

Revised Date: 6 July 2021

Accepted Date: 20 July 2021

Please cite this article as: Levy I, Wieder – Finesod A, Litchevsky V, Biber A, Indenbaum V, Olmer L, Huppert A, Mor O, Goldstein M, Sapir E, Hod T, Cohen C, Lustig Y, Rahav G, Immunogenicity and safety of the BNT162b2 mRNA Covid-19 vaccine in people living with HIV-1, *Clinical Microbiology and Infection*, https://doi.org/10.1016/j.cmi.2021.07.031.

CLM-21-21428

Immunogenicity and safety of the BNT162b2 mRNA Covid-19 vaccine in people living with HIV-1

Itzchak Levy[1,2], Anat Wieder – Finesod[1,2], Vladyslav Litchevsky[1], Asaf Biber[1,2], Victoria Indenbaum[3], Liraz Olmer[4], Amit Huppert[4], Orna Mor[2,3], May Goldstein[1], Einav Sapir[2,6], Tammy Hod[2,5], Carmit Cohen[6], Yaniv Lustig[2,3]*, Galia Rahav[1,2]*

1) The Infectious Diseases Unit, Sheba Medical Center, Tel-Hashomer, Israel.
2) Sackler Faculty of Medicine, Tel-Aviv University, Israel
3) Central Virology Laboratory, Ministry of Health and Sheba Medical Center, Tel-Hashomer, Israel
4) Bio-statistical and Bio-mathematical Unit, The Gertner Institute of Epidemiology and Health Policy Research, Sheba Medical Center, Tel-Hashomer, Israel
5) Nephrology Department, Sheba Medical Center, Tel-Hashomer, Israel
6) The Infection Prevention & Control Unit, Sheba Medical Center, Tel Hashomer, Israel

*These authors contributed equally to this work.

Corresponding author:
Itzchak Levy
Infectious Diseases Unit
Sheba Medical Center
Tel-Hashomer
Phone: +972-3-5304937 Fax: +972-3-5304935
E-mail: itsik.levy@sheba.health.gov.il

Abstract

Objectives: The immunogenicity and safety of the Pfizer-BioNTech BNT162b2 mRNA vaccine in people living with HIV-1 (PLWH) are unknown. We thus aimed to assess the immunogenicity and safety of this vaccine in PLWH.

Methods**:** In this prospective open study, we enrolled 143 PLWH, aged ≥18 years, who attended our clinic and 261 immunocompetent health care workers (HCWs). SARS-CoV-2 receptor binding domain (RBD) IgG and neutralizing antibodies were measured. Adverse events, viral load and CD4 cell counts were monitored.

Results: At a median of 18 days (IQR 14-21) after the second dose, anti-RBD IgG was positive in 139/141 (98%) PLWH. Among HCWs, 258/261 (98.9%) developed anti-RBD IgG at a median of 26 (IQR 24-27) days after the second dose. Following the second dose, immune sera neutralized SARS-CoV-2 pseudo-virus in 97% and 98% of PLWH and HCW, respectively. Adverse events were reported in 60% of PLWH, mainly pain at the injection site, fatigue, and headache. AIDS-related adverse events were not reported. HIV viral load increased in 3/143 (2%) patients from < 40 copies/mL to ≤ 100 copies/mL. CD4+ T cell count decreased from a geometric mean of 700 (95% CI 648–757) cells per µL to 633.8 (95% CI 588–683) cells per µL (P<0.01).

Conclusions: BNT162b2 mRNA vaccine appears immunogenic and safe in PLWH who are on ART with unsuppressed CD4 count and suppressed viral load.

Introduction

The Pfizer-BioNTech BNT162b2 mRNA vaccine has been tested for safety and efficacy in a multinational randomized placebo controlled trial with more than 40,000 participants.[1] In that trial, 196 immunologically stable HIV-1 positive patients were included, but data for the safety and immunogenicity of the vaccine specifically for that patient group have not been published. Indeed, to the best of our knowledge, there are no data available for the response of people living with HIV (PLWH) to mRNA vaccines.

The BNT162b2 mRNA vaccine was introduced in Israel on December 19th, 2020, and our program to vaccinate PLWH started a day later. Since the initiation of the vaccination program in Israel, more than 52% aged 16 and over have been vaccinated.

In this study, we examined the immunogenicity and safety of the BNT162b2 mRNA vaccine in 143 PLWH.

Methods

Study population

The HIV clinic at the Sheba Medical Center serves about 1500 ambulatory patients. . The enrollment into the study was offered to all adult patients (>18 years) who consented to be vaccinated and to participate in the study. Patients who had recovered from SARS-CoV-2 or had active infection at the time of the vaccination (as evident by positive PCR on respiratory swabs or per history) were excluded. Socio-demographic details and clinical and laboratory data regarding HIV status and comorbidities were extracted from computerized medical records. Controls were 261 immunocompetent healthcare workers (HCWs) that were tested for antibody response 2–3 weeks following the second vaccine.

IRB approval was obtained from ethical review boards of the Sheba medical center (7982-20-SMC for PLWH and 8008-20-SMC for immunocompetent HCW). Written informed consent was obtained from all participants.

Immunogenicity was evaluated with an enzyme-linked immunosorbent assay (ELISA) that detects IgG antibodies against the receptor-binding domain (RBD) of SARS-CoV-2[2,3]. Titers ≥1.1 were defined as positive. In addition, a SARS-CoV-2 pseudo-virus (psSARS-2) neutralization assay was performed to detect SARS-CoV-2 neutralizing

antibodies (NA) using a green fluorescent protein (GFP) reporter-based pseudotyped virus with a vesicular stomatitis virus (VSV) backbone coated with the SARS-CoV-2 spike (S) protein [generously provided by Dr. Gert Zimmer (Institute of Virology and Immunology (IVI), Mittelhäusern, Switzerland]. Following titration, 100 focus forming units (ffu) of pseudo SARS-2 were incubated with a twofold serial dilution of heat-inactivated (56°C for 30 min) tested serum. Following incubation, the virus/serum mixture was transferred to Vero E6 cells and incubated for 90 min at 37°C. Plates were incubated for 24 hr and 50% plaque reduction titer was calculated by counting green fluorescent foci using a fluorescence microscope (EVOS M5000, Invitrogen). Sera not capable of reducing viral replication by 50% at a 1 to 8 dilution or below were considered non-neutralizing.

HIV viral load was determined with Cepheid Xpert® HIV-1 Viral Load, where < 40 copies/mL is considered undetectable. CD4 + and CD8 + T cell counts were determined by flow cytometry analysis in peripheral blood.

All clinical adverse events, including local and systemic reactions, were monitored and recorded. Both solicited and unsolicited events were recorded up to three weeks after the second injection.

Continuous variables are presented as means and standard deviation or as geometric means and 95% confidence intervals (CI). Categorical variables are presented as N (%). Differences between groups were assessed using a Chi-square test and a *t*-test, for categorical and continuous data, respectively. A mixed model repeated measures analyses were applied to estimate changes in parameters (CD4, VL, CD4/CD8) at four time points: baseline, after the first and after the second dose and four months after second dose.

The log-transformed of IgG and neutralizing antibodies were analyzed as a continuous variable by using multivariate linear regression. A P-value of <0.05 was considered statistically significant. Statistical analysis was performed in SAS version 9.4 (SAS Institute, Cary, NC, USA).

The correlation between IgG and neutralizing antibodies and CD4 or CD4/CD8 ratio with IgG and neutralization antibodies (log transformed) were analyzed using Spearman's correlation by two-tailed parametric t-test means with confidence interval (CI) of 95%.

Results

Baseline characteristics

Our cohort included the first 143 PLWH who were vaccinated with the BNT162b2 mRNA vaccine in our clinic between 20 December 2020 and 27 January 2021. The average time between first and second dose was 21 days (range 15-31). (Table 1). The control group included 261 immunocompetent HCW that were checked for antibody response 26 (24-27) days after the second vaccine dose. Among PLWH there were more males compared to the control group (91.6% versus 25.3%, p<0.0001). The majority (80%) being men having sex with men (MSM). PLWH were younger than the control (49.8 ± 11.6 versus 55.8 ± 14.3 years, p< 0.0001). Mean BMI in PLWH was similar to the controls (25.1±3.8 versus 25.6 ± 4.4, p=0.3027). PLWH had less comorbidities than controls (11.2% versus 39.1%, p<0.0001). HIV associated parameters in PLWH are presented in Table 2. 18.2% (n=26) had AIDS at HIV diagnosis or later; the average time from HIV diagnosis to vaccination was 13 years. At the time of vaccination, all patients were on anti-retroviral therapy (ART), most of them with integrase inhibitors-based therapy. 95% of PLWH had an undetectable viral load, with baseline geometric mean (GM) CD4+ T cell count of 700 cells per µL (95% CI 648–757). Sixteen (11.2%) patients had comorbidities, 7 had malignancies (4 with solid organ malignancy and 3 with lymphoma), and 2 patients had kidney transplants.

Compared to the entire HIV population attending the Sheba clinic, the study group was significantly older (49.8±11.5 vs 43.2±12.7; p<0.0001) and included more males (92% vs 81.5%, p<0.05) and more MSM (80% vs 38%, p<0.01). People of Sub Saharan African origin were underrepresented (4.2% vs 16% p<0.01). Nevertheless, the time from HIV diagnosis (12.9 vs 12.5 years), CD4+ T cell count on diagnosis (GM 443 vs 470 cells per µL), nadir CD4+ T cells (GM 315 vs 340 cells per µL) and baseline CD4+ T cells prior to vaccination (GM 700 vs 702 cells per µL) were not significantly different between the two groups.

Immunogenicity following BNT162b2 vaccination

Antibody responses after the second vaccine dose are summarized in table 3 and figure 1. 139/143 (97%) PLWH developed RBD-IgG antibodies at a median of 18

(IQR 14-21) days after the vaccine with a GMT of 5.17 (95%CI 4.84–5.53). In the control group, 258/261 (98.9%) developed antibodies after the second dose at a median of 26 (IQR 24–27) days, with a GMT of 6.1 (95%CI 5.8, 6.4). Linear regression analysis, adjusted for age, sex, BMI, comorbidities and number of days after vaccination revealed that PLWH developed lower IgG levels than controls (p=0.008) (table 4a).

131/135 (97%) PLWH developed NAs after the second dose with a GMT of 449 versus 482.8 among controls (Table 3). Adjusted Linear regression analysis revealed that PLWH developed NA 24% less than control (Table 4b). There was a significant correlation [r = 0.46 (95%CI 0.31, 0.59) (p<0.0001)] between RBD IgG antibodies and NAs (Figure 2). Only four patients did not develop NAs, specifically, a 66-year-old man with a kidney transplant treated with mycophenolate, tacrolimus and prednisone, a 58-year-old man on hemodialysis, a 72-year-old man with ischemic heart disease, and a 64-year-old woman with nonspecific arthritis who was treated with colchicine and developed severe COVID-19 four weeks after the second dose of the vaccine.
No correlation between CD4 or CD4/CD8 ratio and IgG nor neutralization titer were found (all log transformed, by Spearman correlation).

Safety

Local adverse effects were more common following the first vaccine (40.6% vs 25.6%), while systemic adverse effects were more common following the second vaccine (19.5% vs. 47.9%) (Table S2). The most common local reaction was pain at the injection site (39% and 23.9% after the first and second doses, respectively), which was mild in most cases and subsided within 24 hours. Fatigue and headache were the most common systemic adverse effects after the first dose, whereas fatigue and fever were the most common adverse effects after the second dose. In most cases the fever was < 38℃, and < 10% required antipyretics.

HIV-related events following vaccination

None of the subjects developed clinical HIV-related events or AIDS defining conditions following vaccination, with 18 (IQR 14-21) days follow days after the second dose.

CD4+ T cell count and HIV-1 viral load following vaccination

Among the PLWH the GM of the CD4 + T cell count decreased significantly from a geometrical mean (95%CI) of 700 (648-757) to 531 (429-657) following the first, 634 (588-683) following the second doses (p=0.0089 between baseline and before 2nd vaccine) and 581 (523-645) 125 ±24 days after the second vaccination (p < 0.0001 relatively to baseline before vaccination). However, the counts remained stable between the first and the second doses and 4 month later. This significant drop in CD4 cell count persisted after adjustment for age, sex, origin, body mass index (BMI), number of years living with HIV, current or past AIDS, and HIV viral load.

The GM of the CD4 +/CD8 + T cell ratio did not change significantly between baseline, first and second doses and 4 month later 0.93 (0.85-1.03), 0.96 (0.78-1.17), 0.929 (0.84-1.017), and 0.85 (0.76-0.96), respectively.

In three patients the viral load increased after the second dose from undetectable levels (< 40 copies/mL) to 47, 52, and 92 copies/mL. In three subjects who had low level viremia (LVV) at baseline, the viral load did not change significantly following vaccination. Four month after vaccination one patient out of 87 (1.15%) blipped to 159 copies/mL, a week later it dropped to 60 copies/mL, no drug resistance mutations were revealed and we continue to follow this patient closely.

All measurements of CD4, CD8 and viral load were done on the same cohort of patients.

Discussion

In our study, the BNT162b2 vaccine was found to be immunogenic and safe in PLWH. However our study population included stable and older HIV-1 positive subjects, mostly with longstanding HIV, treated with integrase inhibitor, have undetectable viral load and current high CD4 + cell count.

Importantly, although it seems that PLWH may have lower RBD IgG antibody levels compared to immunocompetent HCWs, 97-98% of PLWH did develop antibodies after second vaccination and their neutralizing activity was similar to the control.

Although we still do not know the significance of the small discrepancy between RBD IgG levels in PLWH relatively to controls, most of the PLWH developed neutralizing activity similar to controls, and this serves better as a correlate of immunity than total anti RBD IgG antibodies[4]. Nevertheless, in our study there was a high correlation between RBD IgG antibodies and NAs.

For HIV patients, it is imported to collect data on immunogenicity because the cell-mediated and B-cell immune abnormalities that occur as HIV infection advances may reduce the magnitude of the response and the durability of the protection. Nonetheless, several studies have demonstrated the protective benefit of vaccinations against influenza[5,6] and *Streptococcus pneumonia*,[7,8] even in advanced HIV patients. Although efficacy data are sparse for other types of vaccine, studies using surrogate endpoints (most commonly post-vaccination antibody levels) have shown that most HIV patients do generate antibody responses post vaccination.

In our cohort, only three patients had a current CD4 count of <200 cells per μL, but all developed high levels of RBD -IgG antibodies and NAs in response to vaccination.

We found a statistically significant decrease in CD4+ T cell count between baseline levels and those measured following the first and second vaccines, as well as four months after the second vaccination. This drop was not associated with any clinical signs or symptoms, but it should be further monitored. It should be noted that the study was conducted among PLWH who were stable on ART with unsuppressed CD4 count and suppressed VL. A drop in CD4 count may be deleterious for people whose CD4 count is already low, and may not recover as rapidly in people who are not stable on ART.

A similar drop in CD4+ T cell count was not reported in other studies on different types of vaccinations; for example, two studies that examined CD 4+ T cell dynamics in PLWH receiving the 7-valent pneumococcal conjugate vaccine (PCV-7) did not find significant changes in CD4+ count in response to the vaccine at 6 months[9] and 3–4 months[10] post vaccination. In addition, a large study evaluating influenza immunizations in over 30,000 HIV patients found no long-term negative effects on CD4 counts, HIV RNA levels, or progression to AIDS or death.[11]

In our study, HIV-1 viral load increased in 3 subjects from undetectable (< 40 copies/mL) to LLV (< 100 copies/ml) immediately after vaccination. These patients had

nadir CD4+ counts of < 200 cells per µL and also had viral failures, which may imply an increased reservoir. These "blips"[12] are usually not considered as viral failure, and are not rare among PLWH, occurring in about a quarter of patients on stable ART with undetectable viral loads.[13] A transient increase in HIV-1 viral load was also detected two weeks following influenza vaccination in well-controlled patients with HIV[14]; that study found a concomitant decrease in proviral DNA and memory phenotype CD4+ cells and claimed that the elevated viral load could suggest mobilization of a latent reservoir.

We found that the BNT162b2 mRNA Covid-19 vaccine was safe. None of the patients developed an immediate or delayed type hypersensitivity reaction. 40.6% and 25.6% developed local following the first and second doses, respectively, but in most cases they were mild to moderate and subsided after 24–48 hours. Although safety data was not collected for controls at the time that the study was conducted, the rate of adverse events that we found among PLWH was lower than that reported for the Pfizer phase 2/3 trial, with the difference probably being due to the different way in which adverse events were monitored.

The main limitations of this study include lack of appropriated control, small size and limited follow up.

Matched case control study in which PLWH were matched to HCWs according to the exposure was not feasible due to differences in age and sex. Since the blood in the PLWH and the controls was drawn for serologic response at different time points in windows that do not overlap we have adjusted the groups in multivariable linear regression not only for age, sex and comorbidities but also for timing of serology from the second vaccine dose. It should be also stated that in former studies age and sex had a limited effect on antibody production[15].

The small size and limited follow up do not enable us to check for efficacy of the vaccine in PLWH.

In conclusion, this prospective study thus demonstrates the immunogenicity and safety of the BNT162b2 mRNA vaccine in a stable cohort PLWH with a preserved immune system.

Transparency declaration

We declare that we have no conflict of interest.

Author contributions

IL, ES, YL and GR were involved in the study design and supervision; IL, AWF, VL, AB, MG, ES, TH, and CC were involved in data collection; VI, OM, and YL performed the laboratory work; LO and AH performed the data analysis; All the authors were involved in writing the paper and have approved the final version.

Acknowledgments

This Article reports independent research funded by the Sheba medical center. We thank Professor Eyal Leshem M.D. and Professor Gili Regev M.D. for their helpful suggestions, to Ms. Inez Mureinik for language editing and the volunteers who participated in this study.

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Table 1: Baseline characteristics of PLWH and controls vaccinated with BNT162b2 mRNA vaccine.

Variable	PLWH (N=143)	Controls (N=261)	P value
	N (%)	N (%)	
Male/Female (% male)	131/12 (91.6)	66/195 (25.3)	<.0001
Age *mean* ± SD	49.8 ± 11.6	55.8 ± 14.3	<.0001

BMI *mean* ± SD	25.1 ± 3.8	25.6 ± 4.4	0.3027
Comorbidities*, total N (%)	16 (11.2)	102 (39.1)	<.0001
Days** after 1st vaccination, Median (IQR)	15 (14-19)	NA	NA
Days*** after 2nd vaccination, Median (IQR)	18 (14-21)	26 (24-27)	<0.001

* Comorbidities included hypertension, diabetes mellitus, dyslipidemia, ischemic heart disease, chronic obstructive pulmonary disease, kidney disease and liver disease. (Details are presented in Table S1) PLWH –patients living with HIV, CG1 – control group 1, CG2 – control group 2, N – number, SD – standard deviation, IQR – interquartile range, NA – not available, BMI – body mass index. NA – not applicable

** - Refers to days between 1st vaccination and 1st blood drawn for serological, virological and immunological studies

*** - Refers to days between 2nd vaccination and 2nd blood drawn for serological, virological and immunological studies

.

Table 2: HIV related variables (N=143)

Variable	N (%)
Caucasians, n(%)	137 (95.8%)

Africans, n(%)	6 (4.2%)
Time from HIV diagnosis, years, mean (range)	13.2 (0-36)
>15 years since HIV diagnosis, n(%)	48 (33.5%)
AIDS on diagnosis, n(%)	26 (18.2%)
Nadir CD4+ T cells per µL, mean (range)	345 (2-900)
Nadir CD4+ T cell < 100 cells per µL	14 (9.8%)
Nadir CD4+ T cell < 200 cells per µL	25 (17.5%)
Nadir CD4+/CD8+ ratio, mean (range)	0.46 (0.03-1.24)
Viral load on diagnosis copies/mL, mean (range)	626, 518 (42-13M)
Integrase inhibitors, n (%)	135 (94.4%)
2DR	27 (18.9%)

2DR – 2 drug regimen

Table 3. RBD- IgG and neutralizing antibodies (NA) following second vaccine dose, GMT

Study group	Positive RBD-IgG, n/N (%)	RBD-IgG GMT (95% CI)	Positive NA/positive RBD-IgG	NA* GMT (95% CI)
Controls**	258/261 (98.9)	6.1 (5.8- 6.4)	197/201 (98)	482.8 (410.8-567.5)
HIV-1	139/143 (97.2)	5.2 (4.8–5.5)	131/135 (97)	449.0 (366.6-550.0)

*Only samples with neutralizing antibodies titers above the cutoff (>8) were included in the analysis for GMT-NA,

** Controls - healthcare workers without immunosuppression

RBD - receptor binding domain, GMT- geometric mean titer, Vx - vaccination, CL - confidence interval, HIV-1 - human immunodeficiency virus -1,

Table 4a: Multivariate linear regression analysis of predictors of RBD-IgG levels (log transformed) following 2nd vaccination (N=374*)

Variable	Ratio of mean (95% CI)			P
Male	0.99	0.84	1.17	0.95
Age	1.00	0.99	1.00	0.35
BMI	0.99	0.97	1.01	0.25
Days after 2nd vaccine	1.00	0.99	1.01	0.80
Comorbidities	1.01	0.85	1.19	0.93
HIV	0.76	0.62	0.93	0.008

Number of participants: 143 PLWH, 261 Controls, 30 BMI missing

Table 4b: Multivariate linear regression analysis of predictors of neutralizing antibodies levels (log transformed) following 2nd vaccination (N=301)

Variable	Ratio of mean (95% CI)			P
Male	0.76	0.55	1.06	0.11
Age	0.98	0.97	1.00	0.006
BMI	1.04	1.01	1.08	0.02
Days after 2nd vaccine	0.96	0.94	0.99	0.005
Comorbidities	0.58	0.41	0.83	0.003
HIV	0.67	0.45	1.01	0.055

Table S1: Comorbidities among PLWH and controls

Variable	PLWH (N=143)	Control (N=261)	
			p value
Hypertension, N (%)	2 (1.4)	59 (25)	<.0001
Diabetes non-insulin dependent N (%)	0 (0)	23 (9.7)	0.0001
Dyslipidemia N (%)	0 (0)	29 (12.3)	<.0001
Ischemic Heart Disease N (%)	0 (0)	13 (5.5)	0.0043
COPD N (%)	14 (4)	8 (3.4)	0.3
Renal disease N (%)	3 (2.1)	1 (0.4)	0.12
Chronic dialysis N (%)	1 (0.7)	0 (0)	
Hepatic disease N (%)	8 (5.6)	2 (0.8)	0.005
Non AIDS linked malignancies N (%)	2 (1.4)	0 (0)	
AIDS linked malignancies N (%)	7 (4.9)	NA	

COPD chronic obstructive pulmonary disease, NA not applicable

Table S2: Local and systemic reactions reported within 21 days after injection of BNT162b2

Adverse event (AE)	**Total cohort N=143 n(%)**	
	After first dose (N=133)	**After second dose (N=121)**
Any AE	**64 (48.1)**	**60 (49.6)**
Any local AE	54 (40.6)	31 (25.6)
Pain at the injection site	52 (39)	29 (23.9)
Injection-site redness	1(0.7)	1 (0.8)
Injection-site swelling		1 (0.8)
Any systemic AE	26 (19.5)	60 (47.9)
Fatigue	12 (9)	52 (42.9)
Fever	4 (3)	48 (39.6)
Headache	6 (4.5)	14 (11.6)
Myalgia	5 (3.7)	9 (7.4)
Chills	2 (1.5)	9 (7.4)
Paraesthesia	1 (0.75)	2 (1.64)
Upper respiratory tract symptoms	3 (2.25)	0
Arthralgia	2 (1.5)	0
Diarrhoea	2 (1.5)	1 (0.82)
Transient increase in transaminases	0	2 (1.64%)
Amaurosis fugax	1 (0.75)	0
Palpitations	0	1 (0.82)

Legends of Figures

Figure 1: Quantitation of IgG and neutralizing antibodies following the second dose of the BNT162b2 vaccine in PLWH and healthy controls. A) RBD-IgG levels B) Neutralizing antibodies. Horizontal dotted black lines indicate limit level of positive antibodies. The short black lines indicates GMT and 95% CI.
RBD= Receptor Binding Domain. S/CO=sample/cutoff ratio

Figure S1: Correlation of IgG and Neutralizing antibodies. The correlation was analyzed following the second vaccine dose. Horizontal and vertical dotted black lines indicate limit level of positive IgG and neutralizing antibodies, respectively. RBD= Receptor Binding Domain. S/CO=sample/cutoff ratio.

Table 1: Baseline characteristics of PLWH and controls vaccinated with BNT162b2 mRNA vaccine.

Variable	PLWH (N=143)	Controls (N=261)	P value
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Male/Female (% male)	131/12 (91.6)	66/195 (25.3)	<.0001
Age *mean* ± SD	49.8 ± 11.6	55.8 ± 14.3	<.0001
BMI *mean* ± SD	25.1 ± 3.8	25.6 ± 4.4	0.3027
Comorbidities*, total N (%)	16 (11.2)	102 (39.1)	<.0001
Days after 1st vaccination, Median (IQR)	15 (14-19)	NA	NA
Days after 2nd vaccination, Median (IQR)	18 (14-21)	26 (24-27)	<0.001

* Comorbidities included hypertension, diabetes mellitus, dyslipidemia, ischemic heart disease, chronic obstructive pulmonary disease, kidney disease and liver disease. (Details are presented in Table S1) PLWH –patients living with HIV, CG1 – control group 1, CG2 – control group 2, N – number, SD – standard deviation, IQR – interquartile range, NA – not available, BMI – body mass index. NA – not applicable

.

Table 2: HIV related variables (N=143)

Variable	N (%)
Caucasians, n(%)	137 (95.8%)
Africans, n(%)	6 (4.2%)
Time from HIV diagnosis, years, mean (range)	13.2 (0-36)
>15 years since HIV diagnosis, n(%)	48 (33.5%)
AIDS on diagnosis, n(%)	26 (18.2%)
Nadir CD4+ T cells per µL, mean (range)	345 (2-900)
Nadir CD4+ T cell < 100 cells per µL	14 (9.8%)
Nadir CD4+ T cell < 200 cells per µL	25 (17.5%)
Nadir CD4+/CD8+ ratio, mean (range)	0.46 (0.03-1.24)
Viral load on diagnosis copies/mL, mean (range)	626, 518 (42-13M)
Integrase inhibitors, n (%)	135 (94.4%)
2DR	27 (18.9%)

2DR – 2 drug regimen

Table 3. RBD- IgG and neutralizing antibodies (NA) following second vaccine dose, GMT

Study group	Positive RBD-IgG, n/N (%)	RBD-IgG GMT (95% CI)	Positive NA/positive RBD-IgG	NA* GMT (95% CI)
Controls**	258/261 (98.9)	6.1 (5.8- 6.4)	197/201 (98)	482.8 (410.8-567.5)
HIV-1	139/143 (97.2)	5.2 (4.8–5.5)	131/135 (97)	449.0 (366.6-550.0)

*Only samples with neutralizing antibodies titers above the cutoff (>8) were included in the analysis for GMT-NA,

** Controls - healthcare workers without immunosuppression

RBD - receptor binding domain, GMT- geometric mean titer, Vx - vaccination, CL - confidence interval, HIV-1 - human immunodeficiency virus -1,

Table 4a: Multivariate linear regression analysis of predictors of RBD-IgG levels (log transformed) following 2nd vaccination (N=374*)

Variable	Ratio of mean (95% CI)			P
Male	0.99	0.84	1.17	0.95
Age	1.00	0.99	1.00	0.35
BMI	0.99	0.97	1.01	0.25
Days after 2nd vaccine	1.00	0.99	1.01	0.80
Comorbidities	1.01	0.85	1.19	0.93
HIV	0.76	0.62	0.93	0.008

Number of participants: 143 PLWH, 261 Controls, 30 BMI missing

Table 4b: Multivariate linear regression analysis of predictors of neutralizing antibodies levels (log transformed) following 2nd vaccination (N=301)

Variable	Ratio of mean (95% CI)			P
Male	0.76	0.55	1.06	0.11
Age	0.98	0.97	1.00	0.006
BMI	1.04	1.01	1.08	0.02
Days after 2nd vaccine	0.96	0.94	0.99	0.005
Comorbidities	0.58	0.41	0.83	0.003
HIV	0.67	0.45	1.01	0.055

Table 5: HIV variables at base line and after first and second vaccination

Variable	Base line (BL)	After 1st dose	*P* BL to post 1st dose	After 2nd dose	*P* post 1st dose to post 2nd dose	*P* BL to post 2nd dose
CD4+ T cells/mm^3 (geometric mean (95%CI)	700 (648-757)	531 (429-657)	0.0089	634 (588-683)	0.8177	<0.0001
CD4+/CD8+ ratio	0.93 (0.85-1.03)	0.96 (0.78-1.17)	0.2793	0.929 (0.84-1.017)	0.0655	0.2931
Patients with undetectable viral load, n/N (%)	134/141 (95%)	28/29 (96.5%)	0.84	136/142 (95.7%)	0.987	0.35

Fig 1

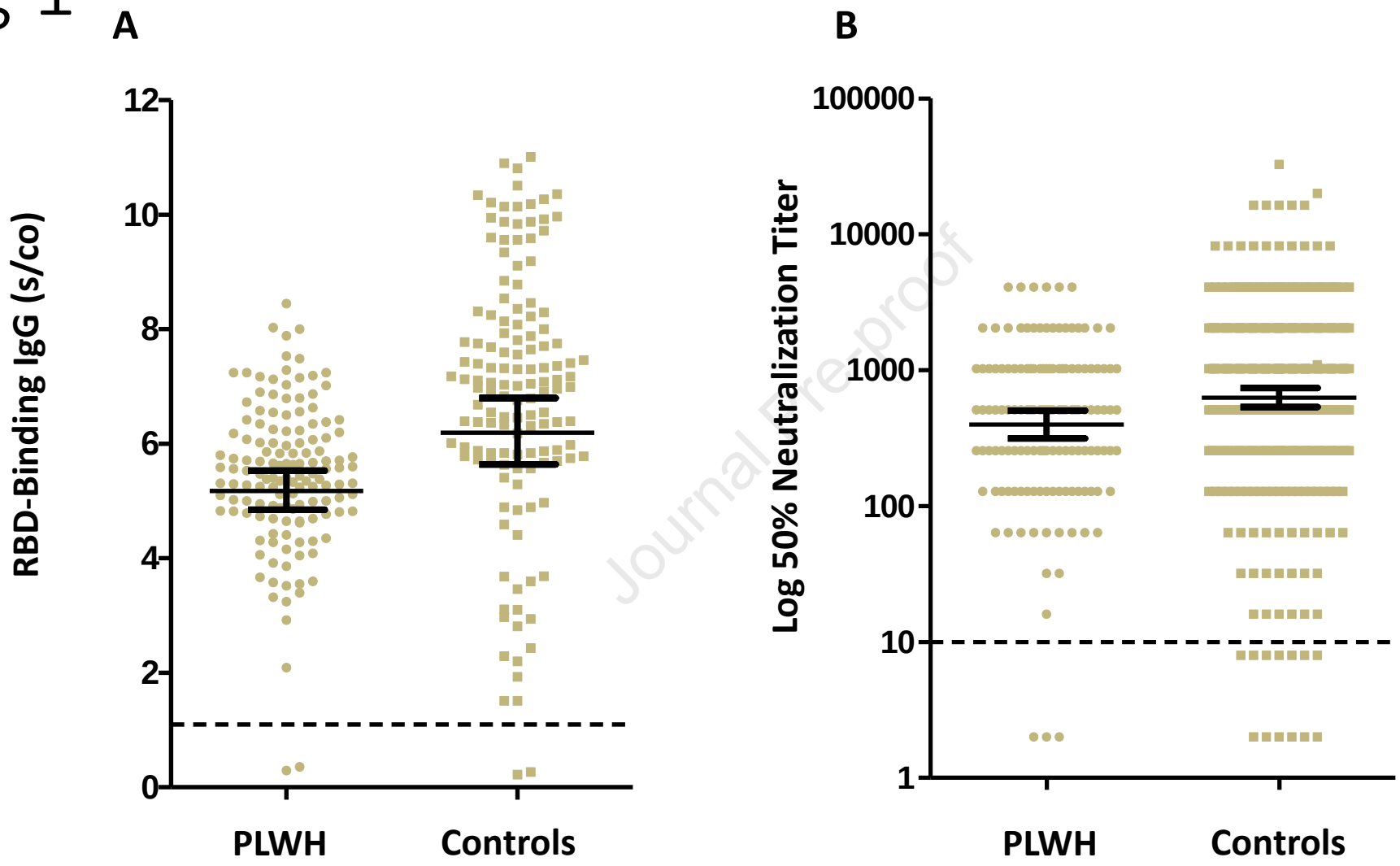

Fig S1