SARS-CoV-2 Vaccine Immunogenicity in PLWH in The Netherlands

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BACKGROUND

Vaccines can be less immunogenic in people living with HIV (PLWH). So far, the immune response after SARS-CoV-2 vaccination of PLWH is not well-established.

METHODS

A prospective cohort study in 22 HIV treatment centres in the Netherlands examined the immunogenicity of SARS-CoV-2 vaccines in PLWH. Included were adult PLWH without prior COVID-19 infection, invited by the national vaccination programme to receive the BNT162b2, mRNA- 1273, ChAdOx1-S or Ad26.COV2.S vaccine. Data from HIV-negative healthy controls were acquired from two concurrent prospective vaccination trials. The primary endpoint was the anti-SARS-CoV-2 IgG response (Liaison Trimeric Spike IgG in BAU/ml) measured 4-6 weeks after vaccination with one of the 2 mRNA vaccines in PLWH versus controls. Secondary endpoints. included antibody response according to sex, CD4+ T-cell count, and vaccine reactogenicity.

		HC (N=440)	PLWH (N=1154)
Vaccine	BNT162b2	94 (21.4%)	884 (76.6%)
	mRNA-1273	247 (56.1%)	100 (8.7%)
	ChAdOx1-S	26 (5.9%)	150 (13.0%)
	Ad26.COV2.S	73 (16.6%)	20 (1.7%)
Sex assigned at birth	Male	126 (28.6%)	987 (85.5%)
	Female	314 (71.4%)	167 (14.5%)
Age category	18-55	352 (80.0%)	703 (60.9%)
	56-65	74 (16.8)	291 (25.2%)
	65+	14 (3.2%)	160 (13.9%)
On cART	Yes	NA	1142 (99.0%)
	No	NA	12 (1.0%)
HIV viral load (copies/ml)	<50	NA	1127 (97.7%)
	≥50	NA	26 (2.3%)
CD4+ T cell count (cells/µL)	<250	NA	41 (3.6%)
	250-500	NA	224 (19.4%)
	>500	NA	889 (77.0%)
CD4 T-cell count nadir † (cells/µL)	<250	NA	443 (38.4%)
	250-500	NA	376 (32.6%)
	>500	NA	152 (13.2%)

Table 1: Characteristics of healthy controls (HC) and people living with HIV (PLWH). Data are n (%), NA: not applicable, † when available

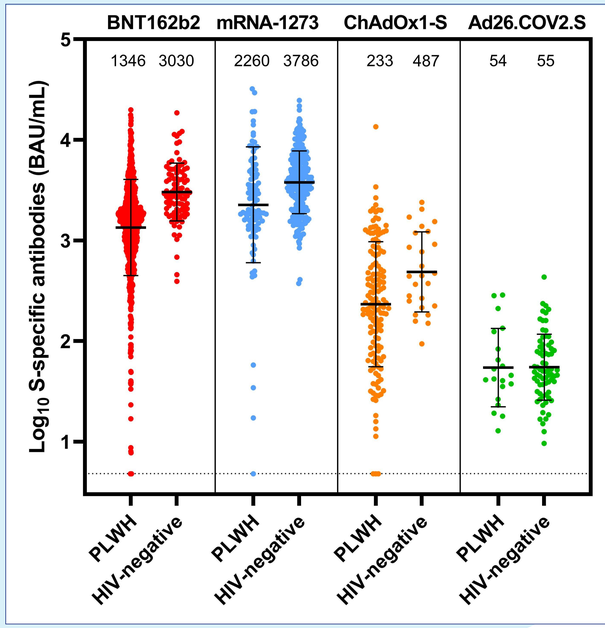


Figure 1: Antibody concentration measured as spike (S)-specific binding antibodies per millilitre (BAU/mL) with BNT162b2, mRNA-1273, ChAdOx1-S and Ad26.COV2.S vaccines in people living with HIV (PLWH) and HIV-negative control group. The thick horizontal bar shows the geometric mean concentration, also indicated above the graphs, with error bars showing geometric standard deviation. The dotted line shows the lower limit of detection of the performed test (4.81 BAU/mL)

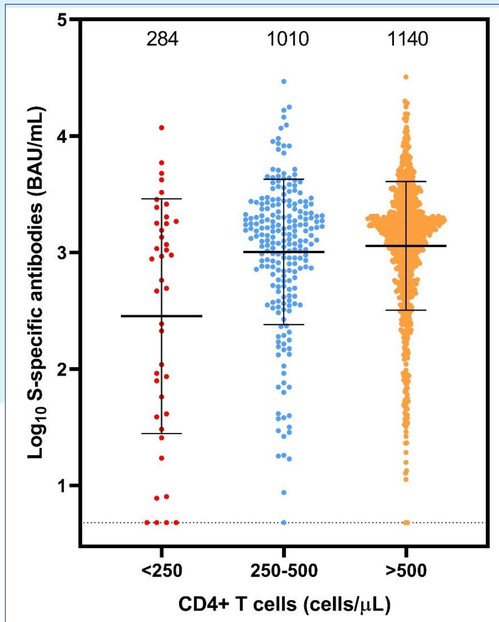


Figure 2: Antibody concentration measured as spike (S)-specific binding antibodies per millilitre (BAU/mL) people living with HIV (PLWH) with different CD4+ T cell counts (in cells/µL). Annotations as stated in figure 1.

RESULTS

Between February 14th 2021 and September 7th 2021, 1269 PLWH were enrolled in the study. At baseline sampling before vaccination, 53 (4.2%) participants had SARS-CoV-2 antibodies detectable in serum and were excluded. 62 (4.9%) were excluded due to other reasons such as loss to follow-up. 1154 PLWH and 440 healthy controls were included in the per protocol analysis. Baseline characteristics of participants can be found in table 1.

The overall geometric mean concentration (GMC) of anti-SARS-CoV-2 antibodies in serum in PLWH was 1060 BAU/mL, which was lower than the GMC of the control group (1585 BAU/ml) (Figure 1). In a multivariate regression analysis in all participants receiving an mRNA vaccine, being HIV positive, an age >65 years and being male were all independently associated with a lower antibody concentration (all $p<0.001$), whilst receiving the mRNA-1273 vaccine was significantly associated with a higher antibody concentration ($p<0.001$). In a multivariate regression analyses including all PLWH receiving mRNA vaccines, receiving an mRNA-1273 vaccine and having a most recent CD4+ T cell count between 250 and 500 cells/µL or higher than 500 cells/µL (all $p<0.001$) were significantly associated with a higher antibody response (Figure 2). Being male ($p=0.001$), having a viral load over 50 copies/ml ($p=0.001$) or being more than 65 years of age ($p<0.001$) were significantly associated with lower antibody responses. CD4+ T cell nadir was not significantly associated with the height of the antibody response.

Reactogenicity occurred in 55 and 50% after the first and second vaccination respectively. When AE occurred, most AE were mild (56.8%) or moderate (32.5%) in severity and self-limiting.

CONCLUSIONS

- After vaccination with BNT162b2 or mRNA-1273, anti-Spike IgG levels were lower in PLWH compared to healthy controls.
- In PLWH, a CD4+ T cell count above 250cells /µL was associated with higher antibody concentrations.
- Additionally, PLWH with a viral load over 50 copies/ml or being of an age over 65 were associated with lower antibody responses
- Side effects in PLWH were similar to phase 3 vaccine studies and were generally mild
- After mRNA vaccination, PLWH of an older age, with lower CD4+ T cell counts and/or detectable viral load can be expected to have a lower degree of protection against COVID-19 and may benefit from a third vaccination.

ACKNOWLEDGEMENTS

We would like to thank all participants and all members of the COVIH study group, without whom this study would not have been possible.