

The BNT162b2 mRNA Vaccine Elicits Robust Humoral and Cellular Immune Responses in People Living with HIV

Bezawit A. Woldemeskel,¹ Andrew H. Karaba¹, Caroline C. Garliss¹, Evan J. Beck², Kristy H. Wang¹, Oliver Laeyendecker², Andrea L. Cox^{^1}, Joel N. Blankson^{#1}

1. Department of Medicine, Johns Hopkins Medicine, Baltimore, MD, USA
2. Division of Intramural Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Baltimore, MD, USA

Corresponding author: 855 N Wolfe Street. Rangos 552. Baltimore MD 21205, USA.

jblanks@jhmi.edu

^ Alternate corresponding author: 855 N Wolfe Street. Rangos 551. Baltimore MD 21205, USA.

acox@jhmi.edu

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Abstract

Previous studies have shown that certain vaccines induce suboptimal responses in people living with HIV (PLWH). However, responses to SARS-CoV-2 vaccines have not been fully characterized in these patients. Here we show that the BNT162b2 vaccine induces robust immune responses comparable to responses in healthy donors.

Keywords: PLWH, COVID, SARS-CoV-2, mRNA vaccine

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Introduction

The BNT162b2 mRNA vaccine induces robust and protective humoral and cellular response to the SARS-CoV-2 spike protein (1) and provides protection from infection with SARS-CoV-2 (2). However, prior studies have shown suboptimal responses to some vaccines in people living with HIV (PLWH) (3). A recent study demonstrated that the ChAdOx1 nCoV-19 (AZD1222) vaccine was effective at inducing humoral and cellular immune responses in PLWH (4), but few studies have addressed the immunogenicity of mRNA vaccines in these patients (5, 6). Here, we determined the capacity of the BNT162b2 mRNA vaccine to induce effective cellular and humoral immune responses in PLWH.

Methods

We obtained blood between 7 and 17 days after the second vaccine dose from 12 PLWH (7 women, 5 men) and 17 healthy donors (7 women, 10 men). None of these individuals had evidence of prior SARS-CoV-2 infection by history or by serology as described below. Informed consent was obtained from all study participants. All PLWH were on antiretroviral therapy and had a median CD4+ T cell count of 913 cells/ul (range of 649 to 1678 cells/ul). Eleven of the 12 PLWH were African American. 3 participants had low level viremia despite being on ART (supplementary Table). Peripheral blood mononuclear cells (PBMCs) and plasma were isolated from whole blood using ficoll centrifugation. We determined cellular immunity to the SARS-CoV-2 spike protein by performing an interferon-gamma (IFN- γ) Elispot assay with unfractionated PBMCs that were stimulated with a pool of overlapping SARS-CoV-2 spike peptides as previously described (7). The assay was also performed with CD8+ T cell depleted PBMCs to determine the relative contribution of CD4+ T cells and CD8+ T cells to the cellular immune response. The titer of SARS-CoV-2 spike binding antibodies was determined with the Euroimmun Anti-SARS-CoV-2 IgG ELISA (Mountain Lakes, NJ). Antibodies to the nucleocapsid protein were measured with the Bio-Rad Platelia SARS-CoV-2 Total Ab assay (Marnes-la-Coquette, France) and used to rule out natural infection with SARS-CoV-2 as mRNA for the nucleocapsid protein is not included in the vaccine. Measurement of antibodies in plasma that block

SARS-CoV-2 Spike binding to ACE2 was performed with the MSD V-PLEX SARS-CoV-2 Panel 6 kit from Meso Scale Diagnostics (Rockville, MD) using a 1:100 dilution of plasma. Differences in Elispot and Euroimmun values were assessed using a two-tailed t-test. Differences in ACE2 blocking between groups was determined by a two-tailed Wilcoxon-Mann-Whitney test with a Bonferroni correction, employing R version 4.05. P-values < 0.05 were considered significant.

Results

There was no significant difference in titers of SARS-CoV-2 spike binding antibodies in healthy donors (median value of 9.49) and PLWH (median value of 8.84 p=0.07) (Figure 1A). Furthermore, healthy donors and PLWH had similar levels of neutralizing antibodies to the vaccine strain spike protein (Figure 1B) and spike proteins from variants of concern (VOC) including the D614G, alpha (B.1.1.7), beta (B.1.351), and gamma (P.1) strains (Figures 1B-F). We next compared the cellular responses elicited by overlapping peptides from the vaccine strain spike protein in PLWH, to responses we obtained in healthy donors from a prior study (7). There was no significant difference in the number of IFN- γ spot forming units or in the stimulation index (values normalized to media alone) between healthy donors and PLWH in unfractionated PBMCs (Figure 1G, H) or with CD8+ T cell depleted PBMCs (Supplementary Figure 1). Finally, the breadth of the T cell response was comparable in the two groups and the similar peptide pools were targeted by the two study groups (Figure 1I).

Discussion

Our study is limited by the relatively small number of participants in both cohorts. While we screened participants for antibodies to nucleocapsid to rule out prior natural infection, the half-life of antibodies to this protein is relatively short (8). Thus we may have missed cases of prior SARS-CoV-2 infection. However, our data confirm a prior study showing that mRNA vaccines induce antibody responses in PLWH (5) and extend the findings by showing that the level of binding

antibodies is not significantly different from that produced in healthy donors. These data are similar to results obtained in a phase 2/3 clinical trial in which the ChAdOx1 nCoV-19 (AZD1222) vaccine was shown to elicit strong SARS-CoV-2 specific antibody and T cell responses in PLWH (4). Of note, in a prior study of naturally infected individuals, antibody titers based on Euroimmun values above 8 were only seen in the top 10% of individuals, and were highly correlated with the highest levels of neutralizing titers based on a microneutralization assay (9). We also demonstrate that neither the magnitude and breadth of vaccine elicited T cell responses nor the breadth of neutralizing antibodies, as determined by responses to spike proteins from wild type virus and VOCs, is significantly different between PLWH and healthy donors. These findings are particularly impressive as the PLWH study participants (median age 52 years, range 25 to 59) were older than the healthy donors (median age 41 years, range 24 to 59) and the BNT162b2 vaccine induces a lower antibody titer in older individuals (10). However, this vaccine also elicits a higher antibody titer in women compared to men (10) and our PLWH cohort had a higher frequency of female participants. Of note, prior vaccine studies in PLWH focused mainly (6) or exclusively on men (4). Data from our balanced cohort strongly suggest that the BNT162b2 vaccine will lead to protection from COVID-19 in men and women living with HIV. Further studies will be needed to determine whether PLWH with lower CD4 T cell counts have the same robust humoral and cellular responses to the vaccine.

Notes:

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Potential Conflicts of Interest

The authors have no conflicts of interest.

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Figure legend

Figure Titer of SARS-CoV-2 spike binding antibodies from healthy donors (HD) and PLWH (A). The horizontal line represents the 90th percentile titer in patients with natural infection. Titer of neutralizing antibodies to spike proteins from vaccine strains SARS-CoV2 (B) and variants of concern (C-F). Spot forming units (G) and stimulation indices (H) to SARS-CoV-2 spike peptide pools from PBMCs from vaccinated PLWH. The black horizontal bars represents the median value for PLWH. The dashed red horizontal bar represents the median value for vaccinated healthy donors (HD) from a prior study (reference 7). The dashed black horizontal lines denote a significant response (SFU>20 and SI >3). Breadth of CD8-depleted T cell responses from PLWH to pools of 10 peptides that sequentially cover the entire spike protein (E). Horizontal bars represent the median values for PLWH, the red horizontal line represents the HD median value.

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Figure 1

