Safety of the Third Dose

To the Editors:

SARS-CoV-2 may exist longer in vivo and further be more likely to mutate and evolve in advanced HIV infection. Therefore, it is crucial to protect people living with HIV (PLWH) from SARS-CoV-2 infection. Booster vaccination is needed because of the waning immunity to primary two-dose COVID-19 vaccines and the immune response weakened by SARS-CoV-2 infection.1,2 In our previous study, we found that the early humoral immune responses to primary two-dose inactivated COVID-19 vaccines in PLWH were weaker than those in healthy individuals, and the adverse reactions between the 2 groups were comparable.3 Currently, it is still unclear whether PLWH will benefit more from a booster dose of inactivated COVID-19 vaccines. Here, we conducted a prospective study to evaluate the early antibody responses and safety of the third dose inactivated COVID-19 vaccines among PLWH on stable antiretroviral therapy.

PLWH and healthy controls (HCs) who were aged between 18 and 59 years and had no SARS-CoV-2 infection history before the first dose inactivated COVID-19 vaccination were enrolled in our study. The third dose inactivated COVID-19 vaccines (Sinopharm, Wuhan Institute of Biological Products Co. Ltd) were administered between October 17, 2021, and December 31, 2021, with an interval of 6 months from the second dose vaccination. Plasma samples were collected at day 14 after the second dose, before the third dose within 7 days, and at day 14 and day 28 after the third dose vaccination. The SARS-CoV-2 neutralizing antibodies (nAbs) against the spike protein receptor-binding domain (RBD) were evaluated with an in-house SARS-CoV-2 nAbs assay kit (Livzon, China). An in-house–developed ELISA kit (Livzon, China) and an in-house–developed colloidal gold kit (Livzon, China) were performed to detect total specific immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies against SARS-CoV-2 recombinant nucleocapsid (N) and RBD antigens. The study was approved by the Research and Ethics Committee of Zhongnan Hospital, Wuhan University, P. R. China (2020079K-1).

A total of 41 PLWH and 18 HCs were enrolled. The median age in the PLWH group and the HC group had no significant difference [38 [interquartile range (IQR) 33–47] vs. 32 (IQR 30–45) years old]. The proportion of males in the PLWH group was higher than that in the HC group (88% vs. 55%, P = 0.016). All PLWH were on antiretroviral therapy, and 37/41 (90.2%) of PLWH reached virological suppression. The baseline median CD4+ T-lymphocyte counts (CD4 count) before the third dose vaccination among PLWH were 542 (IQR 422–643) cells/μL. Of them, 2 (4.8%) had a CD4 count of <200 cells/μL.

The SARS-CoV-2–specific antibody responses before, as well as at day 14 and day 28 after the third dose vaccination between PLWH and the HC group were compared (shown in Fig. 1A–C). The geometrical mean titer (GMT) of nAbs against RBD antigen at day 14 was significantly lower in the PLWH group than that in the HC group [39.010 (95% CI: 21.380 to 71.160) vs. 100.800 (95% CI: 40.280 to 252.300) BAU/mL, P = 0.010]. At day 28 after the third dose, the GMT of nAbs in the PLWH group was still lower than that in the HC group, although there was no statistical significance. The GMT of IgM in the PLWH group was significantly lower than that in the HC group at day 14 [0.020 (95% CI: 0.014 to 0.030) vs. 0.040 (95% CI: 0.022 to 0.072) ELISA units (EU)/mL, P = 0.025] but similar to the HC group before and at day 28 after the third dose. The GMT of IgG in the PLWH group was significantly lower than that in the HC group at both day 14 [0.761 (95% CI: 0.495 to 1.168) vs. 1.335 (95% CI: 0.807 to 2.208) EU/mL, P = 0.035] and day 28 [0.787 (95% CI: 0.523 to 1.183) vs. 1.506 (95% CI: 0.974 to 2.328) EU/mL, P = 0.039] after the third dose. The seroconversion rate of nAbs at day 14 after the third dose in the PLWH group was 92.6% (95% CI: 82% to 100%) and in the HC group was 100%. The seroconversion rate of nAbs at day 14 after the third dose between the HC group and the PLWH group had no significant difference.

The antibody responses at day 14 after the second dose and at day 14 after the third dose were compared among PLWH (shown in Fig. 1D–F) and the HC group (shown in Fig. 1G–I). In the PLWH group, the GMT of nAbs (P = 0.002) and IgG (P < 0.001) at day 14 after the third dose was significantly higher than that at day 14 after the second dose. Similarly, the GMT of nAbs (P = 0.007) and IgG (P = 0.006) in the HC group at day 14 after the third dose was significantly higher than that at day 14 after the second dose. The total adverse reactions within 14 days after the third dose vaccination between the

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than that in healthy individuals, which may be related to the impaired antigen-specific B-cell and T-cell response in PLWH. Consistent with the previous studies in general population with booster inactivated or mRNA COVID-19 vaccination, we found the level of nAbs and IgG was significantly higher and increased rapidly at day 14 after the third dose inactivated COVID-19 vaccines compared with that at day 14 after the second dose and at day 14 after the third dose in HCs. Limited by the short follow-up, the trend and duration of humoral responses after the third dose vaccination in PLWH will continue to be observed. Moreover, no HIV-related events were observed within 28 days after the third dose vaccination. The efficacy of booster inactivated COVID-19 vaccines has been widely concerned. Our study provides the evidence of its early efficacy in PLWH. We indicated that significant humoral immunity, including SARS-CoV-2–specific nAbs, IgM, and IgG, was induced within 14 days after the third dose inactivated COVID-19 vaccines, no matter in PLWH or in healthy individuals. However, the level of nAbs at day 14 and day 28 after the third dose in PLWH was still lower than that in healthy individuals, which may be related to the impaired antigen-specific B-cell and T-cell response in PLWH. Consistent with the previous studies in general population with booster inactivated or mRNA COVID-19 vaccination, we found the level of nAbs and IgG was significantly higher and increased rapidly at day 14 after the third dose inactivated COVID-19 vaccines compared with that at day 14 after the second dose. All those suggest that the immune memory will induce a boost humoral response for the inactivated COVID-19 vaccine in both healthy individuals and PLWH.

Limited by the short follow-up, the trend and duration of humoral responses after the third dose vaccination in PLWH will continue to be observed. Moreover, the SARS-CoV-2–specific cellular immunity will be measured in our further study to supplement the immune protection of the third dose inactivated COVID-19 vaccines.

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