Effectiveness of COVID-19 primary and booster vaccination in HIV-infected individuals

Bin Su[a] and Guido Vanham[b]

See related paper on page 709

AIDS 2023, **37**:837–839

People with HIV (PWH) are affected by various degrees of immune deficiency and they often present co-morbidities and therefore could be at higher peril for complicated SARS-CoV-2 infection. HIV infection is indeed associated with more severe COVID-19 and death in Africa than in North America, while there is less of a difference between PWH and HIV-negative controls in Europe, Asia, and South America, probably reflecting the different degree of viral control and immune reconstitution of PWH in these regions [1]. In a large South African cohort for instance, untreated HIV-infected COVID-19 patients were more likely to die in hospital [2]. Importantly, Cele *et al.* [3] documented a chronic SARS-CoV-2 infection in a South African patient with advanced HIV disease, which evolved extensive immune escape, thus potentially becoming a source of a new immune-evasive SARS-CoV-2. Therefore, for both individual and public health reasons, PWH are a priority target population for vaccination [4].

How effective are COVID-19 vaccines in inducing immune responses and protection against SARS-CoV-2 infection in PWH?

A review of 22 studies with 6522 PWH demonstrates that, after the second dose, seroconversion in PWH was slightly lower than that in healthy individuals [5]. The trend to lower immune responses in PWH cohorts compared with HIV-negative populations are in line with reports on other vaccines, for example, against influenza or hepatitis B virus [6].

A more detailed analysis in European studies demonstrates that seroconversion rate, anti-Spike antibodies, and neutralizing titers in PWH with $CD4^+$ T-cell counts over 500/μl were comparable with those in healthy controls, while they were clearly reduced in individuals with $CD4^+$ T cells below 200/μl, even when these patients received a fully viral-suppressive antiretroviral treatment [7–10]. Similarly, South African PWH under stable treatment but with incompletely suppressed viral load (under 1000 copies/ml) responded well to full vaccination with either recombinant Spike protein (Novavax) or chimp adenovector (Astra-Zeneca) vaccines but with lower titers [11,12].

The Canadian COVAXHIV Study Team performed the first study on real-world effectiveness during the pre-Omicron era, using a test-negative approach in over 21 000 well-treated PWH, vaccinated with two doses of BNT162b2, mRNA-1273, or ChAdOx1 vaccines. They found a very similar protection against infection and severe disease among these PWH as compared to HIV-negative subjects [13]. Similarly, the single-dose Ad26.COV2.S vaccine (Johnson & Johnson) showed a good effectiveness against COVID-related hospitalization and death during the beta and delta wave in South African healthcare workers, including those who were HIV-positive [14].

[a]Beijing Key Laboratory for HIV/AIDS Research, Sino-French Joint Laboratory for Research on Humoral Immune Response to HIV Infection, Clinical and Research Center for Infectious Diseases, Beijing Youan Hospital, Capital Medical University, Beijing, China, and [b]Global Health Institute, University of Antwerp, Campus Drie Eiken, Gouverneur Kinsbergencentrum, Wilrijk, Belgium.

Correspondence to Guido Vanham, Global Health Institute, University of Antwerp, Campus Drie Eiken, Gouverneur Kinsbergencentrum; Doornstraat 331, 2610 Wilrijk, Belgium.

E-mail: gvanham@itg.be

Received: 10 January 2023; accepted: 16 January 2023.

DOI:10.1097/QAD.0000000000003492

Obviously, PWH, regardless of their $CD4^+$ T-cell count, are eligible to receive additional vaccine doses, but what is the response to boosters?

In a Belgian cohort, a third dose of mRNA vaccine considerably enhanced SARS-CoV-2 specific humoral and cellular immunity in PWH. Humoral responses were similar between PWH and HIV(−) individuals. However, although SARS-CoV-2 specific IFN-gamma production increased after the third dose, it remained significantly lower among SARS-CoV-2 naive PWH compared with HIV(−) controls [15]. In a Dutch cohort of PWH with a hypo-response after a primary vaccination regimen, an additional dose of mRNA-1273 induced a robust serological response in 64 of 66 PWH after 1 month, including neutralizing antibodies to wild-type virus, as well as T-cell responses, regardless of the primary vaccination regimen or patient characteristics [16]. A German study found that, after the second and the third vaccination, the titers of neutralizing antibodies against wild-type SARS-CoV-2 were slightly reduced in PWH compared with controls, but the reduction against Delta and Omicron variants was more pronounced. Despite the reduced $CD4^+$ T-cell count in the peripheral blood of PWH, the $CD4^+$ T cellular response to COVID-19 vaccination was preserved. During the follow-up, eight out of 71 PWH acquired a breakthrough infection (BTI) after the second dose and six additional ones after the third dose, but no details on severity were provided [17].

In this issue of AIDS, Lapointe *et al.* explore [18] the response to a booster even more extensively in a Canadian cohort. They showed a similar durability of immune responses over a 6 months period in PWH under suppressive treatment as in healthy controls. WT-specific and Omicron-specific IgG concentrations, ACE2 displacement, and virus neutralization declined at similar rates among PWH and healthy controls who remained SARS-CoV-2-naïve. BA.1-specific neutralization was undetectable in more than 80% of COVID-19 naive PWH and more than 90% of controls. BTI boosted antibody concentrations and function significantly above vaccine-induced levels in both PWH and healthy controls, though BA.5-specific neutralization remained significantly poorer than BA.1, suggesting the need for a second booster in both PWH and healthy controls [18]. Unfortunately, no details on the severity of BTI is provided.

In conclusion, virally suppressed PWH with high $CD4^+$ T-cell counts respond well to the primary course of various COVID-19 vaccines, but those with lower $CD4^+$ T-cell counts have lower levels of SARS-CoV-2-specific immune responses. Recent data, including those by Lapointe *et al.* in this issue, show that the magnitude and durability of the response to a booster in PWH with high $CD4^+$ T-cell counts are also rather comparable with those in healthy controls, while information on SARS-CoV-2 specific T-cell responses is apparently inconsistent between studies [15,17]. Omicron sub-variant responses were very weak after 6 months in both PWH and healthy controls.

The data on real-world effectiveness are limited, but both a Canadian and a South African study in the pre-Omicron era were reassuring in that PWH do not suffer from more frequent or more severe COVID-19 BTI than matched healthy controls after two doses. No clear comparison on the frequency and severity of BTI after a third dose in PWH and HIV(−) controls has been described yet.

Since Omicron sub-variants are increasingly escaping vaccine-induced and infection-induced immunity, PWH should be advised to take additional sub-variant-adapted boosters, as soon as they become available. Further studies in PWH should be performed to elucidate the potential impact of various immunization strategies in this population according to their disease status and outcome [19].

Acknowledgements

The current work was supported by the Beijing Natural Science Foundation (L222068) and the Beijing Key Laboratory for HIV/AIDS Research (BZ0089). The funders had no role in study design, data collection, and analysis, decision to publish, or preparation of the article.

Conflicts of interest

There are no conflicts of interest.

References

1. Oyelade T, Alqahtani JS, Hjazi AM, Li A, Kamila A, Raya RP. **Global and regional prevalence and outcomes of COVID-19 in people living with HIV: a systematic review and meta-analysis.** *Trop Med Infect Dis* 2022; **7**:22.
2. Jassat W, Cohen C, Tempia S, Masha M, Goldstein S, Kufa T, *et al*. **Risk factors for COVID-19-related in-hospital mortality in a high HIV and tuberculosis prevalence setting in South Africa: a cohort study.** *Lancet HIV* 2021; **8**:e554–e567.
3. Cele S, Karim F, Lustig G, San JE, Hermanus T, Tegally H, *et al*. **SARS-CoV-2 prolonged infection during advanced HIV disease evolves extensive immune escape.** *Cell Host Microbe* 2022; **30**:154–162.
4. Mandala WL, Liu MKP. **SARS-CoV-2 and HIV-1: should HIV-1-infected individuals in sub-Saharan Africa be considered a priority group for the COVID-19 vaccines?** *Front Immunol* 2021; **12**:797117.
5. Yin J, Chen Y, Li Y, Wang C, Zhang X. **Immunogenicity and efficacy of COVID-19 vaccines in people living with HIV: a systematic review and meta-analysis.** *Int J Infect Dis* 2022; **124**:212–223.
6. Johnston JA, Tincher LB, Lowe DK. **Booster and higher antigen doses of inactivated influenza vaccine in HIV-infected patients.** *Ann Pharmacother* 2013; **47**:1712–1716.
7. Hensley KS, Jongkees MJ, Geers D, GeurtsvanKessel CH, Mueller YM, *et al*. **Immunogenicity and reactogenicity of SARSCoV-2 vaccines in people living with HIV in the Netherlands: a nationwide prospective cohort study.** *PLoS Med* 2022; **19**:e1003979.

8. Corma-Gomez A, Fernandez-Fuertes M, García E, Fuentes-Lopez A, Gomez-Ayerbe C, Rivero-Juarez A, *et al*. **Severe immunosuppression is related to poorer immunogenicity to SARS-CoV-2 vaccines among people living with HIV.** *Clin Microbiol Infect* 2022; **28**:1492–1498.
9. Antinori A, Cicalini S, Meschi S, Bordoni V, Lorenzini P, Vergori A, *et al*. **Humoral and cellular immune response elicited by mRNA vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in people living with human immunodeficiency virus receiving antiretroviral therapy based on current CD4 T-lymphocyte count.** *Clin Infect Dis* 2022; **75**: e552–e563.
10. Hassold N, Brichler S, Ouedraogoa E, Leclerc D, Carroue S, Gater Y, *et al*. **Impaired antibody response to COVID-19 vaccination in advanced HIV infection.** *AIDS* 2022; **36**:F1–F5.
11. Madhi SA, Moodley D, Hanley S, Archary M, Hoosain Z, Lalloo U, *et al*. **Immunogenicity and safety of a SARS-CoV-2 recombinant spike protein nanoparticle vaccine in people living with and without HIV-1 infection: a randomised, controlled, phase 2A/2B trial.** *Lancet HIV* 2022; **5**:e309–e322.
12. Madhi SA, Koen AL, Izu A, Fairlie L, Cutland CL, Baillie V, *et al*. **Safety and immunogenicity of the ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 in people living with and without HIV in South Africa: an interim analysis of a randomised, double-blind, placebo-controlled, phase 1B/2A trial.** *Lancet HIV* 2021; **8**:e568–e580.
13. Chamber C, Samji H, Cooper CL, Costiniuk CT, Janjua NZ, Abigail E, Kroch AE, *et al*. **Coronavirus disease 2019 vaccine effectiveness among a population-based cohort of people living with HIV.** *AIDS* 2022; **36**:F17–F26.
14. Bekker LG, Garrett N, Goga A, Fairall L, Reddy T, Yende-Zuma N, *et al*. **Effectiveness of the Ad26.COV2.S vaccine in healthcare workers in South Africa (the Sisonke study): results from a single-arm, open-label, phase 3B, implementation study.** *Lancet* 2022; **399**:1141–1153.
15. El Moussaoui M, Lambert N, Braghini J, Gofflot S, Toussaint F, Vermeersch P, *et al*. **Reduced T-cell response following a third dose of SARS-CoV-2 vaccine in infection-naïve people living with HIV.** *J Infect* 2022; **85**:702–769.
16. Jongkees MJ, Geers D, Hensley KS, Huisman W, Geurtsvan-Kessel CH, Bogers S, *et al*. **Immunogenicity of an additional mRNA-1273 SARS-CoV-2 vaccination in people living with HIV with hyporesponse after primary vaccination.** *J Infect Dis* 2022:jiac451[Online ahead of print].
17. Bessen C, Plaza-Sirvent C, Simsek A, Bhat J, Marheinecke C, Urlaub-Bessen D, *et al*. **Impact of SARS-CoV-2 vaccination on systemic immune responses in people living with HIV.** *Front Immunol* 2022; **13**:1049070.
18. Lapointe HR, Mwimanzi F, Cheung PK, Sang J, Yaseen F, Speckmaier S, *et al*. **Antibody response durability following three-dose COVID-19 vaccination in people with HIV receiving suppressive ART.** *AIDS* 2023; **37**:709–721.
19. Jin J, Wang X, Carapito R, Moog C, Su B. **Advances in research on COVID-19 vaccination for people living with HIV.** *Infect Dis Immun* 2022; **2**:213–218.