HIV patients are at increased risk of COVID-19 morbidity and mortality. Moreover, increased SARS-CoV-2 mutation development has been reported in (African) HIV-1 infected patients. Previous reports documented the safety and immunogenicity of mRNA-based SARS-CoV-2 vaccines in people infected with HIV. This is less documented for inactivated SARS-CoV-2 vaccines. In their article published in *ClinicalMedicine*, Feng and colleagues provide preliminary evidence on the safety and immunogenicity of an inactivated SARS-CoV-2 vaccine in HIV patients, one of the first to report on this topic in this patient group who are at increased risk of severe COVID-19.

The paper describes an open-label two-arm non-randomized study, in which the investigators provided two doses of inactivated SARS-CoV-2 vaccine (BIBP-CorV), 4 µg each at an average of 4 weeks apart. Forty-two HIV-1 infected individuals who were stable on potent combination antiretroviral treatment (ART), with CD4 cell counts >200, and the majority (63%) being virologically suppressed were included in the study. In addition, 28 healthy individuals were included as controls. Safety and immunogenicity was investigated by measuring anti-spike IgG levels, surrogate virus neutralization assay, spike protein-specific IFN-Ɣ ELISpot, and T-cell activation responses. Baseline data was compared with data obtained at 4 weeks after the first BIBP-CorV vaccine dose, and 4 weeks after the second dose.

As with mRNA vaccines, Feng and colleagues demonstrated that HIV-1 infected patients who were on stable ART, exhibited similar safety profiles as well as humoral and cellular immune responses as HIV-1 uninfected, after vaccination with an inactivated SARS-CoV-2 vaccine (BIBP-CorV). The investigators did not observe solicited adverse reactions among any of the study participants. There were no differences in binding, and neutralizing antibody levels, as well as spike protein-specific T cell responses elicited between HIV-1 infected individuals and healthy controls. Interestingly, HIV-1 infected individuals with low baseline CD4/CD8 ratio (i.e. <0.6) generated lower antibody responses after inactivated SARS-CoV-2 vaccination compared to those with medium (0.6–1.0) or high (>1.0) baseline CD4/CD8 ratio. The investigators noted also inactivated SARS-CoV-2 vaccine induced immune activation though without a parallel increase in HIV-1 viremia. Another recent report revealed that HIV-1 infected individuals have comparable neutralizing antibody responses to inactivated SARS-CoV-2 vaccine as healthy individuals, but the responses were lower in magnitude, and there were decreased T helper (Th)-2 and Th17 responses to SARS-CoV-2 spike proteins. However, there was no difference in regulatory T cell (Treg) and cytokine responses, including IL-2, TNF-α and IFN-Ɣ responses between HIV-1 infected and healthy controls.

The follow-up in both previous studies is of short duration, and whether the immune responses observed will remain sustained for longer duration of time remains to be elucidated. In addition, immune responses among older patients (>60 years), and those with CD4 cell counts <200 remains to be determined. Failure to seroconvert after vaccination with SARS-CoV-2 mRNA vaccines has been reported. Thus, evaluating the response to inactivated SARS-CoV-2 vaccines among HIV-1 infected individuals with uncontrolled or unsuppressed HIV-1 viral load is also top priority. In addition, immune responses, in particular neutralizing antibody responses against emerging SARS-CoV-2 variants, such as the delta and omicron lineages remains to be elucidated.

Hypermutated SARS-CoV-2 develops during infections of longer duration in patients with suppressed immune system. For this reason HIV-1 patients could represent a source of such variants too. The recent outbreak of Omicron originating from South Africa likely developed in (an) isolated HIV-1 patient(s). Africa as a continent hosts the majority of the world’s HIV-1 patients (25 million), and development of novel SARS-CoV-2 variants that potentially result in higher morbidity and mortality than Omicron cannot be excluded. This is particularly imminent, when vaccination rates remain low and human preventive behavior is

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virtually absent due to the relative ‘invisibility’ of COVID-19 in Africa, as reported by us and others. For the reasons noted above, we would advocate for preferential vaccination of HIV-1 infected populations in settings with low vaccine coverage, such as Africa. The current study by Feng and colleagues is reassuring in this respect, since it indicates that in addition to mRNA vaccines, also inactivated SARS-CoV-2 vaccines are suitable for usage in HIV-1 infected patients. Therefore, we would support integral addition of COVID-19 vaccines to the list of available protective arsenals for people with HIV-1. In addition, it might be worth investigating in future clinical trials the combined use of inactivated SARS-CoV-2 vaccines with other mRNA based vaccines.

Contributors

DW wrote the commentary. TRW reviewed the commentary and provided additional insights.

Declaration of interests

DW is European and Developing Countries Clinical Trials Partnership (EDCTP) Senior Research Fellow, and received funding from EDCTP for the projects Eval-Amp and Profile-Cov; he serves as Strategic and Scientific Advisory Board of the Research Networks for Health Innovations in Sub-Saharan Africa (German Federal Ministry of Education and Research), and has received an honorarium for lectures and presentations from the Ethiopia Ministry of Science and Higher Education. TRW is employee of not-for-profit PharmAccess Foundation, is Board Member of Mondial Diagnostics, and Scientific Advisory Board member of Healthinc, The Netherlands.

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