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48 weeks. The ongoing SALSA study (NCT04021290), a large, international, randomised open label trial, assessing switch from triple ART therapy to a fixed-dose combination of dolutegravir plus lamivudine, will provide further insight into the efficacy and safety of switch in this population. Although dual therapy offers promise of reduced medication exposure and reduced side effects, as well as the potential to be cost saving, additional evidence from long-term studies including data on women and non-White populations are needed to determine who will best benefit from these newer strategies.

We declare no competing interests.

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SARS-CoV-2 vaccination in people with HIV

At this point in the COVID-19 pandemic, with vaccine roll-out ongoing, the most urgent question facing people with HIV and their health-care providers is whether HIV modulates the immune response to and subsequent effectiveness of the SARS-CoV-2 vaccines in preventing severe COVID-19 disease. Data on whether HIV increases the risk of severe COVID-19 are conflicting, with initial studies showing that excess risk was associated with the presence of other comorbidities associated with severe COVID-19.¹ However, subsequent investigations in larger and more diverse population-based cohorts have suggested that people with HIV with lower CD4 cell counts or unsuppressed viral loads might be at increased risk of severe COVID-19.^{1,2} SARS-CoV-2 vaccination is expected to substantially reduce this risk, although there is a paucity of HIV-specific data.

People living with HIV have diminished or less durable response to hepatitis B³ and yellow fever vaccination,⁴ and people with low CD4 cell counts have diminished antibody titres to diphtheria, tetanus, and poliomyelitis.⁵ This lower magnitude or less durable immune response in HIV-positive populations than in the HIV-negative population is thought to be mediated by lower CD4/CD8 ratios, T-cell exhaustion, or persistent inflammation related to HIV infection despite effective antiretroviral therapy (ART).³ After natural infection with

SARS-CoV-2, people with HIV have lower anti-spike IgG concentrations and pseudovirus neutralising titres.⁶ For other immunocompromising conditions, such as solid organ transplantation, decreased immunogenicity to SARS-CoV-2 mRNA vaccination has been documented, with data emerging for other conditions.⁷ Investigators from the Novavax COVID-19 vaccine study's South African sites reported that efficacy decreased from 60% (95% CI 20–80) to 49% (6–73) when people living with HIV were included in the analysis, although these data have not yet been published.⁸ These concerns have led public health authorities to recommend selective use of facemasks and physical distancing after vaccination among immunocompromised individuals until additional data are available.

In *The Lancet HIV*, John Frater and colleagues⁹ present anxiously awaited data on the humoral and cell-mediated response to the ChAdOx1 nCoV-19 prime-boost vaccine among 54 people living with HIV (all male, median age 42.5 years [IQR 37.2–49.8]) compared with 50 adults without HIV. Only individuals with HIV who were virologically suppressed on ART and had CD4 counts of more than 350 cells per μL were enrolled, and the median CD4 count was 694 cells per μL (IQR 574–860). The authors examined humoral immunity by measuring anti-spike IgG concentrations,



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and live virus neutralisation among a randomly selected subset of 15 individuals with HIV, and cell-mediated immunity via ex-vivo IFN- γ enzyme-linked immunospot (ELISpot) and T-cell proliferation studies. Reassuringly, IgG concentrations were similar or higher when examined up to day 56 after prime vaccination (geometric mean ratio 1.66 [95% CI 1.14–2.41] at day 56), and four of 15 individuals showed evidence of SARS-CoV-2 neutralisation by day 28, which increased to 13 of 15 at day 56. Investigation of cell-mediated immunity by HIV status showed no differences in ELISpot responses at all timepoints, with 40 (91%) of 44 individuals with HIV with available data having a response by day 14, and proliferative CD⁺ and CD8 cells to SARS CoV-2 increasing significantly from baseline.

Frater and colleagues' results support that people with HIV who are on effective ART with suppressed viral loads and high CD4 cell counts (>350 cells per μ L) do not have diminished humoral and cell-mediated responses to the ChAdOx1 nCoV-19 prime-boost vaccine, although longer term follow-up is needed to examine the durability of these responses. Increasing data suggest that SARS-CoV-2 seropositivity after natural infection is correlated with later protection,¹⁰ although prospectively following up people with HIV after vaccination will be important. However, we should not attempt to extrapolate these data to people with HIV with lower CD4 counts or CD4/CD8 ratios than the population studied here, or without suppressed HIV viral loads. The diminished humoral immune response after natural infection with SARS-CoV-2 among people with HIV,⁶ but not after ChAdOx1 nCoV-19 vaccination, could be related to the differing populations examined, given that people with HIV with unsuppressed viral loads or low CD4 cell counts were not included in Frater and colleagues' study. Alternatively, the greater immunogenicity of vaccination compared with previous natural infection could attenuate or

reverse differences in the immunological response by HIV status. Future studies will need to enrol diverse populations with HIV to investigate whether the vaccination maintains high efficacy in those with low CD4 cell counts and who are not virally suppressed because they are at greater baseline risk of severe COVID-19. Although these studies are ongoing, these encouraging data support the importance of SARS-CoV-2 vaccination as a principal COVID-19 prevention strategy among people with HIV.

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