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COVID-19 in patients with HIV

We read with interest the report by Blanco and colleagues¹ of five people living with HIV who were admitted to a Barcelona hospital with COVID-19. We believe that caution is required before drawing conclusions on the outcome of COVID-19 in this population.

Evidence is evolving that protease inhibitors developed for the treatment of HIV, both lopinavir and darunavir boosted by ritonavir or cobicistat, are not efficacious against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in vivo.^{2–4} Therefore, antiretroviral combinations should not be changed in an attempt to treat SARS-CoV-2 infection, because neither drug combination is a first-line choice in most guidelines for HIV and changing treatment could lead to increased rates of adverse events.

Antiretroviral treatments such as non-nucleoside reverse transcriptase inhibitors and integrase inhibitors have better tolerability than boosted protease inhibitors.⁵ Moreover, three of the five cases described by Blanco and colleagues were initiated or switched to an antiretroviral combination containing a pharmacokinetic booster, thereby introducing a substantial risk of significant drug-drug interactions.⁵ New antiviral drugs active against COVID-19 are being developed, and interactions of such drugs with

antiretrovirals can be seen frequently. For example, remdesivir might interact with carbamazepine and other drug metabolism inducers, and no data are available on potential interactions with nucleoside analogues used in antiretroviral combinations.⁵

Caution is needed when interpreting the incidence of COVID-19 in people living with HIV compared with the HIV-negative population. The numbers reported by Blanco and colleagues are small and patients attended only one hospital, so the sample is subject to bias. The authors do not report on the proportion of patients with COVID-19 who were tested for HIV infection. Without universal HIV testing, it is not possible to calculate the incidence of the two viral infections occurring in the same individual simultaneously.

The statement that only 1% of people admitted with COVID-19 to one hospital in Barcelona had HIV can be misinterpreted and falsely reassuring, particularly while we still do not entirely understand which populations should be protected from COVID-19 by social interventions, such as shielding, self-isolation, and frequent testing. In the UK, large cohort studies are being done to investigate the true rate of infection, clinical characteristics, and outcomes of COVID-19 in people with HIV.

Challenges in understanding the true frequency of COVID-19 in people with HIV include the overall limited testing that has happened so far, particularly for patients not needing hospitalisation, the admission of patients in hospitals external to where the individual might access their HIV care, and the fact that people with HIV might be more vigilant at shielding and self-isolation because of the propagation of fears of higher acquisition rates and a poorer outcome of SARS-CoV-2 infection in people living with HIV.

Finally, appropriately powered and designed studies are needed to draw conclusions on the effect of COVID-19

in people with chronic diseases, including HIV infection. HIV infection is itself characterised by various clinical scenarios, ranging from viral suppression and good quality of life to HIV-associated comorbidities or virological failure with or without immunosuppression.⁵

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Authors' reply

We thank Rachael Jones and colleagues for highlighting two issues prescribing caution before drawing conclusions from our case series¹ of COVID-19 in HIV-infected patients. The first issue is regarding treatment with boosted protease inhibitors; the second is about

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prevalence of HIV-infected patients at our institution. We appreciate the attention paid to our work and their valuable insight.

First, as Jones and colleagues point out, knowledge about the efficacy of different antiviral treatments against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is evolving rapidly, and local protocols have been periodically updated. When treating the five cases described, we relied on findings of previous in-vitro studies and limited clinical data for efficacy of lopinavir-boosted ritonavir against severe acute respiratory syndrome. Published since that time, a Chinese clinical trial has shown scant efficacy of lopinavir-boosted ritonavir against SARS-CoV-2,² and Janssen published a note³ reporting darunavir has no affinity for the SARS-CoV-2 protease. We agree that boosted protease inhibitors introduce a substantial risk of drug-drug interactions, but our five cases were managed by skilled infectious disease specialists and they presented neither remarkable side-effects nor substantial drug-drug interactions during the 14-day treatment period. At the time of the publication of our case series, patient 2 was still in intensive care, requiring extracorporeal membrane oxygenation, but he survived and was discharged on April 30, 2020, with a plasma RNA HIV viral load below 50 copies per mL and, thus, this patient has reverted to their previous antiretroviral regimen (abacavir, lamivudine, and dolutegravir).

Second, Jones and colleagues question the 1% prevalence of HIV-infected cases admitted with COVID-19. We had stated that our findings were both the first data to be published and preliminary results. Moreover, our local protocol included HIV serology for all hospitalised COVID-19 patients. The 1% prevalence has been confirmed in Barcelona after 2 months. 42 HIV-infected patients with COVID-19 visited the hospital clinic emergency

department, of whom 32 (76%) were admitted and among whom only one new case of HIV was diagnosed. These figures represent 0.7% of the 5649 patients in our institution's HIV cohort, 1.9% of the 2215 emergency department visits, and 1.5% of the 2102 hospital clinic admissions. The prevalence of HIV-infected patients with COVID-19 was, therefore, similar to the findings of a Chinese survey⁴ reporting 0.7% of HIV-infected cases with COVID-19 (eight of 1174), whereas the rate of HIV hospital admissions was slightly higher than the 0.8% (42 of 5700) reported in New York City.⁵

These are preliminary results and we must redouble our efforts, doing appropriate studies to define more clearly the main epidemiological and clinical features of COVID-19 in HIV-infected patients.

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Evolving ART crisis for people living with HIV in Indonesia

Country lockdowns in response to the COVID-19 pandemic are causing drug shortages that are crippling health-care provision for people living with HIV in Indonesia. The supply chain of antiretroviral treatment (ART) has halted amid lockdowns and travel restrictions from India.¹ Many Indonesian districts have completely run out of ART, with other districts running out within 2 weeks. This shortage will result in tens of thousands of people living with HIV stopping ART treatment.

All ART procurement and administration is handled via the Indonesian Ministry of Health, but drugs are procured from outside the country. First-line ART predominantly involves generic fixed-dosed tenofovir, lamivudine, and efavirenz via Mylan (Canonsburg, PA, USA); some supplies are stuck in procurement systems with no further supplies able to come in. Our clinic, a key population HIV/sexual health clinic in Bali, has made provisions to ration tenofovir, lamivudine, and efavirenz to 10 days' supply at once and made switches to zidovudine-based treatment; we have also stopped immediate ART start. At present, all our stocks of drugs will run out within 2 weeks. There has been disconnected local advice to supply patients with mono or dual ART using existing low stocks of nucleoside reverse transcriptase inhibitors (lamivudine and zidovudine) and non-nucleoside reverse transcriptase inhibitors (efavirenz or nevirapine) to keep people going, which would have terrible consequences in driving ART

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