Darunavir does not prevent SARS-CoV-2 infection in HIV patients

In 2003, the screening of approved drugs identified lopinavir, the inhibitor of HIV type 1 aspartate protease, as a potential treatment of severe acute respiratory syndrome (SARS) caused by coronavirus (SARS-CoV) [1,2]. Lopinavir and also darunavir, the most recent HIV protease inhibitor, are the current proposed drugs also for the treatment of COVID-19 caused by SARS-CoV-2 [3]. In this paper we report three HIV-positive subjects on antiretroviral (ARV) regimen containing darunavir with good immunovirological status, diagnosed with COVID-19.

On March 10th 2020, a 62-years-old HIV-positive man was admitted at our emergency department referring dry cough and fever up to 38.8 °C for at least 7 days. His ARV regimen consisted of darunavir/cobicistat 800/150 mg and lamivudine 300 mg once daily. Blood tests performed less than 2 months earlier showed an undetectable viral load (< 20 copies/mL) and a CD4+ count of 0.441 × 10^3/μL. He was also on maintenance therapy with doxazosin, metoprolol and amlodipine for arterial hypertension and ischemic heart disease. Chest x-ray evidenced a bilateral reticular interstitial thickening. No contacts with known cases of COVID-19 were reported by the patient but, considering the ongoing epidemic in Lombardy [4], a nasopharyngeal swab for SARS-CoV-2 was performed retrieving a positive result. Darunavir/cobicistat was replaced by lopinavir/ritonavir plus hydroxychloroquine. In the following days, the patient’s respiratory function quickly worsened despite Venturi mask and continuous positive airway pressure therapy and, one week after admission, the patient required mechanical ventilation. In the intensive care unit lopinavir/ritonavir plus hydroxychloroquine were replaced by tocilizumab (two doses) and remdesivir (withdrawn for acute liver injury after 5 days) with improved respiratory conditions. At the last available follow-up (April 1), the patient is still inpatient with no fever and requiring only low-flow oxygen delivery.

The second case was a 63-years old HIV-infected man on darunavir-based antiretroviral therapy (given at 800 mg coformulated with cobicistat, tenofovir alafenamide and emtricitabine); at the last outpatient visit he had an undetectable viral load (< 20 copies/mL) and a CD4+ count of 0.743 × 10^3/μL. He was also on active treatment with irbesartan for arterial hypertension and raltegravir) and on nebivolole and atorvastatin, developing SARS-CoV infection, have been proposed as a suitable treatment for SARS-CoV-2 infected patient [3]. Lopinavir showed efficacy against SARS-CoV both in patients and in tissue culture, dropped viral titers, and ameliorated disease progression in marmosets infected with MERS-CoV [5,6]. A recent publication in Korea suggested that lopinavir/ritonavir might reduce COVID-19 viral load and improve clinical symptoms [7].

Given the structural similarity with lopinavir, darunavir is a potentially effective treatment against SARS-CoV-2 and is currently under investigation in phase III clinical trials [3]. However, with these clinical reports, we provide preliminary evidence that darunavir, at least at the currently adopted dosage of 800 mg, did not prevent SARS-CoV-2 infection in people living with HIV and, at least in one case, did not protect from the worsening of respiratory function.

Declaration of Competing Interest

There are no conflicts to declare.
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