Avibactam confers susceptibility to a large proportion of ceftazidime-resistant Pseudomonas aeruginosa isolates recovered from cystic fibrosis patients

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Sir,

Pseudomonas aeruginosa is the predominant bacterial pathogen in cystic fibrosis (CF) patients and is associated with decline in pulmonary function.1 Due to the chronic persistent nature of infections, CF patients receive frequent antibiotic courses for eradication of potential pathogens, treatment of acute infectious exacerbations and as chronic suppressive therapy. Consequently, resistance to antipseudomonal β-lactams is common in the strains collected from CF patients.2,3 Narrowing therapeutic options. Clinicians are therefore forced to use aminoglycosides or polymyxins, increasing the risk of adverse effects.4,5 Therefore, optimizing the activity of β-lactams may help to alleviate this burden. Ceftazidime is a well-established cephalosporin (on the WHO List of Essential Medicines) with an excellent safety profile and an antibacterial spectrum that includes P. aeruginosa. However, ceftazidime is degraded by many β-lactamases, including ESBLs (Ambler classes A and D), cephalosporinases (Ambler class C) and carbapenemases. Avibactam (formerly NXL-104) is a novel non-β-lactam, broad-spectrum β-lactamase inhibitor, with promising inhibitory activity against Ambler class A (including ESBLs and Klebsiella pneumoniae carba

References


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strains, a value that is below the EUCAST and CLSI susceptibility breakpoints, extending to CF \(P.\ aeruginosa\) isolates the conclusions obtained for pseudomonal isolates of other origins and for other Gram-negative bacteria.

Taken together, these data highlight the potential utility of combining ceftazidime with avibactam for the treatment of \(P.\ aeruginosa\) infections, including in clinical situations where resistance rates are high. It also shows that a concentration of 4 mg/L is sufficient to bring into the susceptible range those \(P.\ aeruginosa\) strains with a ceftazidime MIC ≤256 mg/L.

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Early ART in primary HIV infection may also preserve lymphopoiesis capability in circulating haematopoietic progenitor cells: a case report

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Sirs,

ART effectively suppresses viral replication and controls infection for an undefined period of time; however, viral eradication is not achievable because of long-lived cellular HIV reservoirs.1,2 We previously showed that, in chronically infected subjects with undetectable plasma HIV-RNA, bone marrow CD34+ haematopoietic progenitor cells (HPCs) are apparently free of HIV replication, but are blunted in differentiation capability,3 and may harbour HIV-DNA even after a long period on successful ART.4 Moreover, in patients treated with successful ART for a very long time, a persistent impairment in the lymphopoietic capability of circulating CD34+ HPCs was found, and lymphopoiesis exhaustion resulted correlated to systemic immune activation, only partially reversed by prolonged ART.5 To date, the mechanisms of HIV-related lymphopoiesis dysfunction remain largely unexplained, and in particular, little information is available on the possibility of limiting the occurrence of irreversible damage by early ART introduction.

We herein describe immune activation levels, T cell profile/response and circulating HPC kinetics in a patient with primary HIV infection receiving early treatment with ART. The patient was further followed for 12 months, and blood samples were analysed before (baseline) and after 2, 24 and 48 weeks of ART. A young adult male was recently diagnosed with HIV acute infection (Fiebig IV stage according to Fiebig et al.). Baseline plasma HIV-1 RNA was 1868262 copies/mL, and CD4+ T lymphocyte count was 389 cells/mm3. Ritonavir-boosted darunavir, tenofovir+emtricitabine and raltegravir were started on day 3 after diagnosis. After 12 weeks of ART, viral load dropped <40 copies/mL and ART was simplified to rilpivirine+emtricitabine+tenofovir. Plasma HIV-RNA remained undetectable at all timepoints thereafter.

The viro-immunological parameters are shown in Figure 1(a). CD4+ cell count steadily increased over time: 534, 1218 and 1072 cells/µL at weeks 2, 24 and 48, respectively. Proviral HIV-DNA, determined as described in Rozera et al.,1 was 82 479 copies/106 PBMC at baseline and 21 534, 17 52 and 6 809 copies/106 PBMC at weeks 2, 24 and 48, respectively. CD8+ T cell activation, measured as CD38 expression by flow cytometry, paralleled plasma HIV-RNA viral load, reaching at week 24 the level found in healthy donors. On the other hand, the level of early CD8+ T cells, evaluated by CD127 expression, steadily increased from baseline to week 48 (Figure 1b).

Peripheral blood CD4++ and CD8++ T cell differentiation was evaluated by CD45RA and CCR7 expression.9 As shown in Figure 1(c), the variation in CD4++ subsets included a decrease in effector memory (EM; CD45RA−/CCR7−) and an increase in...