Second-line Antiretroviral Treatment in Resource-Limited Settings: Abandon Lopinavir/Ritonavir Monotherapy or Search for New Candidates?

To the Editor—We read with great interest the report by Kumarasamy et al [1], which has further extended the A5230 study of the AIDS Clinical Trial Group (ACTG). The ACTG A5230 study initially demonstrated that Lopinavir/ritonavir
(LPV/r) monotherapy is promising for human immunodeficiency virus (HIV)-infected patients failing first-line antiretroviral therapy (ART) in resource-limited settings, with viral suppression achieved in 87% of the patients at week 24 [2]. However, this percentage dropped to 62% at week 104 [1]. The result is consistent with the HIV STAR and EARNEST studies showing inferior viral control with LPV/r monotherapy as second-line therapy [3,4]. Intriguingly, higher treatment failure also occurs in LPV/r monotherapy as first-line therapy ART [5,6]. Therefore, LPV/r monotherapy is not preferred for HIV patients, neither as initial therapy nor as second-line therapy.

When LPV/r monotherapy failed, ACTG A5230 study added emtricitabine/tenofovir (FTC/TDF) [1]. With this strategy, the vast majority of the patients could control their HIV viral load below 400 copies/mL [1]. Although the result is encouraging, we are concerned with its clinical application. As reviewed by Kumarasamy et al in their CID paper [1] and is true in our clinical center, first-line ART failure is often recognized late in resource-limited settings. ART failure is usually suspected when patients have poor CD4 cell recovery or develop new opportunistic infections. At that time, patients are usually very fragile. What they urgently needed is restoring their immune function as quickly as possible. However, the ACTG A5230 study’s strategy will give the virus a chance to continue destroying the already impaired immune system, at least in about 40% of the patients. Indeed, this strategy will save money to some extent, but it may increase the risk of opportunistic infections. In our opinion, it is better to choose a regimen with high effectivity and low resistance potential as second-line ART in resource-limited settings.

In addition, psychosocial factors should not be overlooked. ACTG A5230 study’s strategy not only increases the cost of monitoring but also increases the frequency of hospital visit and the associated absence from work, which may cause job losses. Furthermore, HIV patients suffer stigma, and this may impact medication adherence [7,8]. HIV status is a very important matter of privacy for our patients. Healthcare providers should be aware of whether increasing the frequency of clinical visits is harmful to HIV privacy, although this is true for our patients. In China, there are special hospitals, such as our hospitals, that mainly manage the patients with communicable diseases. Visiting such a kind of hospital too often may be regarded as a sign of having a communicable disease. It is indeed a reason that some of our patients have poor adherence.

Although there are limitations, ACTG A5230 study is worthy of further investigation in special conditions. In our clinical center, the first-line ART regimens for HIV patients are selected from zidovudine (AZT) /TDF+lamivudine (3TC)+ efavirenz/ nevirapine combinations. As TDF is much more expensive than AZT in Nanjing, TDF is reserved for patients not tolerating AZT. Usually, when the TDF-containing regimen has failed, we are unable to use AZT. As ART failure is usually confirmed late in our center, virus may have developed multidrug resistance to TDF+3TC. Nevertheless, TDF+3TC is retained in the second line ART with a third drug LPV/r. However, we are largely uncertain whether in this condition the inclusion of TDF+3TC provides additional viral suppression or is just a waste of money and adds toxicity. Study of this special condition would guide us in making clinical decisions.

Notes

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