First-Line Antiretroviral Therapy in Resource-Limited Settings: Time to Reconsider?

To the Editor—Combination treatment with lamivudine, stavudine, and the non-nucleoside reverse-transcriptase inhibitor (NNRTI) nevirapine is the first-line antiretroviral (ART) regimen recommended by the World Health Organization for the treatment of HIV infection. This regimen is associated with a low genetic barrier to resistance. Therefore, to avoid the development of resistance, its supply must not be interrupted. Strategies have been developed by international nongovernmental organizations (NGOs) to secure the supply of ART to patients, particularly in insecure areas [1]. Is it time, however, to consider boosted protease inhibitor (PI)—based combination therapy as the first-line regimen in certain resource-limited settings (RLS)?

Supply problems lie not with delivery at the national level but in overcoming obstacles to supply at the local level. While working with an international NGO in the Democratic Republic of Congo, we experienced many obstacles to the delivery of ART supplies in an unstable RLS. Civil unrest continues, particularly in the east, where rural health care is scarce. Most patients traveling to our clinics from the villages kept their appointments. But when the patients’ dependents became sick, their crops needed harvesting, or violence erupted in their region, several months sometimes passed between appointments.

Urban health care is provided by state agencies, private agencies, and NGOs. The stability of the supply of medications is uncertain. On occasion, we were approached by the local teaching hospital when their stocks of essential medications ran out. During the first 2 years of the ART program sponsored by our NGO, we were the sole providers of ART in the province. A few months into program, samples of our medications appeared in pharmacies 200 km away.

Lima et al. [2] demonstrated that boosted PI-based ART regimens were significantly associated with a lower emergence of resistance, compared with nonboosted PI-based regimens. This remained the case at all levels of treatment adherence [2]. This trend has also been demonstrated by other recent studies [3]. Patients who start therapy with lower CD4+ cell counts and higher viral loads (which is the case for the majority of HIV-infected persons in sub-Saharan Africa) were also less likely to develop resistance than were those taking a nonboosted PI or an NNRTI [3, 4]. British HIV Association guidelines state that “a boosted protease inhibitor is likely to be preferable for patients with a risk of poor adherence given that treatment with this type of drug is less likely to lead to the emergence of resistance” [5, pp. 2102–2103].

The heat-stable, boosted PI coformulation lopinavir/ritonavir is increasingly available in RLS as a part of second-line combination therapy. As was seen with the current first-line regimen, considerable political will, advocacy, and the possibility of generic combined ART is needed to address the huge price differential. However, these recent findings should cause us to consider whether a first-line NNRTI-based combination is still the best treatment option for patients in certain RLS.

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References
1. Culbert H, Tu D, O’Brien DP, et al. HIV treatment in a conflict setting: outcomes and expe-

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Reconsidering First-Line Antiretroviral Therapy in Resource-Limited Settings: The Need for Operational Research

Adlington et al. [1] suggest that we should consider the use of boosted protease inhibitor regimens instead of nonnucleoside reverse-transcriptase inhibitor-based regimens in certain resource-limited settings. We tend to agree with the authors for the reasons they state, with the proviso that this plan is implemented in settings that actively monitor the relative long-term effectiveness of these treatment strategies in the field.

Public health decisions based solely on efficacy findings from randomized clinical