Although more than 20 years of antiretroviral therapy use has resulted in the selection of multidrug-resistant (MDR) HIV-1, new drugs in the traditional and newer antiretroviral drug classes provide an increasing range of options for the effective treatment of HIV-1 infection.

Crafting an effective regimen for the treatment of MDR HIV-1 infection including a boosted PI, an NNRTI, and an NRTI combination, such as tenofovir/emtricitabine or abacavir/lamivudine, can be a daunting challenge given the paucity of information on the potential pharmacokinetic drug-drug interactions, adverse effects, and interpretation of drug resistance test results. With respect to new approaches to MDR HIV-1, the DUET genotypic data reported by Haubrich and colleagues provide evidence for virological response rates greater than 67% to DRV/r and etravirine among patients with 3 or fewer darunavir or etravirine resistance-associated mutations (RAMs) and less consistent but encouraging response rates of 29% to 65% among patients with up to 6 (combined) darunavir or etravirine RAMs.

Rawizza and Sax present current examples of the choices and conundrums in the treatment of patients with high levels of drug resistance after long and checkered histories of antiretroviral therapy. They pose an important question: what is the appropriate dosing of the first-line NNRTIs, efavirenz and nevirapine, when given with DRV/r in persons with MDR HIV-1 infection? To address this issue, they reviewed the data provided from studies of normal volunteers (HIV-1–uninfected persons). Although most of the interactions between DRV/r and efavirenz or nevirapine increase the NNRTI and darunavir plasma drug levels, the data available sound a note of caution in that interactions may also result in a modest increase in efavirenz levels (and hence, a risk of CNS toxicity) as well as a slight decrease in darunavir levels.

Of the 3 cases presented by Rawizza and Sax, their third patient, who was treated with a combination of DRV/r, etravirine, tenofovir/emtricitabine, and the integrase inhibitor raltegravir, provides a glimpse of the future for treating persons with MDR HIV-1 infection. For patients with successfully suppressed MDR HIV-1 infection who have required the parenterally administered entry inhibitor enfuvirtide to be included in their drug regimen, raltegravir has been successfully substituted with sustained suppression. The results from community-based studies of patients with MDR infection have demonstrated the potency of the integrase inhibitor class. When this new class of antiretroviral drugs has been incorporated into a drug regimen, patients have achieved greater than 90% virological suppression.
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References

Dr Katzenstein reports receiving research grants and serving on advisory boards for Bristol-Myers Squibb, GlaxoSmithKline, Merck, Abbott, Roche, and Gilead.

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