Letters to the Editor

Journal of Antimicrobial Chemotherapy
doi:10.1093/jac/dkn556
Advance Access publication 21 January 2009

Comment on: High rate of early virological failure with the once-daily tenofovir/lamivudine/nevirapine combination in naive HIV-1-infected patients

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Keywords: adherence, resistance, HIV

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Sir,

Rey et al.1 compared nevirapine, lamivudine and tenofovir once daily versus nevirapine, lamivudine and zidovudine twice daily among antiretroviral-naive HIV-infected subjects. Unexpectedly, more early virological failures with resistance occurred with the once-daily regimen, despite higher self-reported adherence levels in this group (71% versus 59% with the twice-daily regimen). This is one of the lowest adherence levels ever reported in a randomized trial aimed at comparing the intrinsic efficacy of two antiretroviral combinations. In my opinion, all hypotheses have not been discussed in the paper.

Compared with once-daily antiretroviral regimens, the twice-daily adherence rate is lower,2 but twice-daily antiretroviral regimens can limit treatment interruptions3—a risk factor for nevirapine or efavirenz resistance.4 In another similar randomized study with higher adherence levels,5 6 out of 39 patients who discontinued the study early had virological failure with resistance to efavirenz, didanosine and lamivudine once daily versus only 1 out of 54 with efavirenz, lamivudine and zidovudine twice daily (P=0.02, by Fisher’s exact test). It is noteworthy that non-inferiority of the once-daily regimen was demonstrated in the end.

The rationalized choice for antiretroviral therapy in clinical practice is usually based on randomized studies conducted among selected subjects with better adherence. Rey et al.1 should be commended for waiving this principle, but their conclusion only applies to the population studied. In my opinion, larger studies with higher adherence are needed to assess the intrinsic efficacy of nevirapine, tenofovir and lamivudine (or emtricitabine) once daily. On the other hand, their report elegantly suggests that the intuitive ‘simpler is better’ for starting antiretroviral therapy among individuals with adherence problems may not always be true.

Transparency declarations

J.-J. P. has received prior grant support from Abbott and Boehringer-Ingelheim.

References


Journal of Antimicrobial Chemotherapy
doi:10.1093/jac/dkp064
Advance Access publication 12 March 2009

High rate of early virological failure with the once-daily tenofovir/lamivudine/nevirapine combination in naive HIV-1-infected patients—authors’ response


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Letters to the Editor

Sir,

Dr Parienti reminds us, in his comments1 on the DAUFIN trial,2 that simpler is not always better, even if the adherence rate was better with once-daily regimens than with twice-daily regimens according to a recent meta-analysis3 (but the effect was only modest and more pronounced at the time of treatment initiation). Treatment interruptions are a risk factor for non-nucleotide reverse transcriptase inhibitor (NNRTI) resistance development, but no difference has been shown when nevirapine was administered once or twice a day.4

More early virological failures with resistance to efavirenz have been observed with didanosine/lamivudine/efavirenz once a day compared with zidovudine/lamivudine + efavirenz twice a day,5 but the adherence rate was not different between treatment arms; therefore, the resistance mutations are probably more associated with the NRTI background choice.

Despite a non-optimal adherence rate with the once-daily regimen in the DAUFIN trial, the high virological failure rate remains unexplained, and the same virological failures have been observed in a study by Lapadula et al.,6 which evaluated the tenofovir, emtricitabine and nevirapine combination, but with a twice-a-day nevirapine administration.

Finally, if we agree that simpler is not always better, on the other hand, it is not worse. According to clinical trials, as well as real life, most of the patients on antiretroviral treatment remain in virological success while more and more combinations are administered once daily.

Transparency declarations

C. A. has received consulting fees from Gilead and GlaxoSmithKline and lecture fees from Bristol-Myers Squibb, GlaxoSmithKline and Merck. All other authors: none to declare.

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