Once-Daily Regimen May Increase Drug Holidays

To the Editor—Molina et al. [1] showed good efficacy and safety of once-daily antiretroviral combination (ARV) therapy during the 24 first weeks of treatment with emtricitabine, didanosine, and efavirenz among 40 patients who were naïve to treatment. Ease of administration of once-daily dosing represents a considerable advance in the quality of life of human immunodeficiency virus (HIV)–infected patients. Molina et al. investigated once-daily highly active antiretroviral therapy regimens as a means of optimizing treatment adherence. However, the impact of once-daily treatment on adherence is not clear from the medical literature.

In a review of 57 publications on the relationship between patient adherence rate and medication dosing across a wide range of chronic illnesses [2], once- and twice-daily regimens were better than 3- or 4-times daily regimens, but once- and twice-daily schedules were similar if we consider treatment adherence as the percentage of drugs taken. Recently, no difference in adherence was observed between nelfinavir given twice a day and efavirenz given once a day [3], although both were given with twice-daily dual nucleoside analogues. On the other hand, a twice-daily regimen is considered to be more reliable than a once-daily regimen if the first dose is missed [4]. In a study that compared once- and twice-daily dosages in clinical practice, Kruse et al. [5] reported that hypertensive patients went without medication for 48 h 3 times more frequently with a once-daily regimen than with a twice-daily regimen (P < .05). Similarly, Paes et al. [6] showed a significantly higher number of 24-h periods without a dose with once-than with twice-daily regimens among patients who were following an oral antidiabetic regimen. Because of an increase number of treatment interruptions among nonadherent patients [7], subtherapeutic ARV drug concentrations followed by HIV RNA rebound may lead to more-rapid K103N mutation, conferring cross-resistance [8] among efavirenz, nevirapine, and delavirdine and compromising a patient’s future treatment options for life. Further studies involving long-term assessment of adherence and follow-up for ARV resistance are needed to assess the clinical impact of once-daily versus twice-daily ARV regimens.

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References


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Reply

To the Editor—We appreciate the letter from Parienti et al. [1] regarding our study [2] on once-daily combination therapy with emtricitabine, didanosine, and efavirenz in human immunodeficiency virus (HIV)–infected patients. Parienti et al. bring to our attention their concern that once-daily regimens may increase drug holidays, thereby favoring the emergence of viral resistance and, eventually, of treatment failure.

In effect, Parienti et al. [1] have raised 2 issues. The first is the impact of once-daily treatments on adherence. They referred to the study by Kruse et al. [3], to suggest that twice-daily regimens are considered to be more reliable than once-daily regimens [3]. However, this observational study was conducted on only 24 patients with hypertension, 9 of whom were receiving a twice-daily regimen [3]. In another study of 91 diabetic patients, Paes et al. [4] showed a clear relationship between compliance and the number of daily doses. Compliance was 98.7%, 83.1%, and 65.8% with once-daily, twice-daily, and 3-times daily regimens, respectively, in that study. It is also our hypothesis that once-daily regimens could be associated with better compliance, which is known to optimize virologic outcome for HIV-infected patients [5].

The second issue raised by Parienti et al. [1] relates to the impact of drug holidays on treatment failures in nonadherent patients to a once-daily regimen. Paes et al. [4] reported that, among nonadherent diabetic patients, the percentage of a 24-h period without therapeutic coverage was higher with a once-daily regimen than with twice- or 3-times daily regimens. This