Failures of 1 week on, 1 week off antiretroviral therapies in a randomized trial

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BACKGROUND: Scheduled treatment interruptions are being evaluated in an effort to decrease costs and side effects of highly active antiretroviral therapy (HAART). A schedule of 1 week on and 1 week off therapy offers the promise of 50% less drug exposure with continuously undetectable HIV RNA concentration. METHODS: In the Staccato study 600 patients on successful HAART were to be randomized to either continued therapy, CD4-guided therapy, or one week on, one week off therapy. A scheduled preliminary analysis evaluated effectiveness in the 1-week-on-1-week-off arm. RESULTS: Of 36 evaluable patients, 19 (53%) had two successive HIV RNA concentrations > 500 copies/ml at the end of the week off therapy, and were classified as virological failure. Most of those who failed took didanosine, stavudine, saquinavir, and ritonavir (11 patients). In these patients, there was no evidence of mutations suggestive of drug resistance, and plasma saquinavir levels were within the expected range. Two of three patients failing on triple nucleotides had drug resistance mutations, but nonetheless responded to reintroduction of triple nucleotide therapy. One of two patients taking nevirapine, and one of eight taking efavirenz, also failed. Both had resistance mutations at the time of failure, but not at baseline. CONCLUSIONS: The 1-week-on-1-week-off schedule, as tested in the Staccato study, showed an unacceptably high failure rate and was therefore terminated.