To the Editor—Two years ago, we reported in this Journal a randomized clinical trial of the tumor necrosis factor-α (TNF-α) inhibitor, pentoxifylline, as adjunctive therapy in human immunodeficiency virus type 1 (HIV-1)-infected persons with pulmonary tuberculosis (TB) [1]. The study found that pentoxifylline therapy resulted in decreased plasma HIV-1 RNA and β2-microglobulin and, in a subset of moderately anemic subjects, improved blood hemoglobin. At the time the study was planned, concern was raised that, given the role of TNF-α in immune defenses against Mycobacterium tuberculosis, inhibition of TNF-α might lead to increased rates of treatment failure or relapse. The report, reflecting 1.5 years of follow-up, did not completely resolve this question, as it noted trends toward increased adverse outcomes in TB therapy in the pentoxifylline arm (7 vs. 2 controls) that did not reach statistical significance.

We recently completed a second analysis of outcomes in this cohort, after nearly 4 years of follow-up. Of the original study subjects, 91% could be included in this analysis; the rest were lost to follow-up. As expected, the number of adverse events has increased significantly with time. However, the trend toward increased adverse events in the pentoxifylline arm has not continued. As indicated in table 1 above, TB adverse events and total deaths do not differ in the two treatment arms. The sample size is sufficient to identify with 80% certainty a 2.8-fold increase in the rate of TB adverse events—less than that observed in the original report.

This represents the longest period of observation of HIV-1–infected subjects with active opportunistic infections treated with a TNF-α inhibitor. It indicates that such treatment does not increase the risks of relapse, other opportunistic infections, or death. However, the extent of the reduction in TNF-α observed with pentoxifylline is modest, as is that for plasma HIV RNA. It is therefore appropriate that future studies of other, more highly active TNF-α inhibitors should similarly evaluate both short- and long-term safety with respect to potential infectious complications of such therapy.

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References

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