Systematic or test-guided treatment for tuberculosis in HIV-infected adults

Conrad Muzoora, Epicentre Mbarara Research Centre, Uganda

Background

In regions with high burdens of tuberculosis and human immunodeficiency virus (HIV), many HIV-infected adults begin antiretroviral therapy (ART) when they are already severely immunocompromised. Mortality after ART initiation is high in these patients, and tuberculosis and invasive bacterial diseases are common causes of death.

Methods

We conducted a 48-week trial of empirical treatment for tuberculosis as compared with treatment guided by testing in HIV-infected adults who had not previously received ART and had CD4+ T-cell counts below 100 cells per cubic millimeter. Patients recruited in Ivory Coast, Uganda, Cambodia, and Vietnam were randomly assigned in a 1:1 ratio to undergo screening (Xpert MTB/RIF test, urinary lipoarabinomannan test, and chest radiography) to determine whether treatment for tuberculosis should be started or to receive systematic empirical treatment with rifampin, isoniazid, ethambutol, and pyrazinamide daily for 2 months, followed by rifampin and isoniazid daily for 4 months. The primary end point was a composite of death from any cause or invasive bacterial disease within 24 weeks (primary analysis) or within 48 weeks after randomization.

Results

A total of 522 patients in the systematic-treatment group and 525 in the guided-treatment group were included in the analyses. At week 24, the rate of death from any cause or invasive bacterial disease (calculated as the number of first events per 100 patient-years) was 19.4 with systematic treatment and 20.3 with guided treatment (adjusted hazard ratio, 0.95; 95% confidence interval [CI], 0.63 to 1.44). At week 48, the corresponding rates were 12.8 and 13.3 (adjusted hazard ratio, 0.97 [95% CI, 0.67 to 1.40]). At week 24, the probability of tuberculosis was lower with systematic treatment than with guided treatment (3.0% vs. 17.9%; adjusted hazard ratio, 0.15; 95% CI, 0.09 to 0.26), but the probability of grade 3 or 4 drug-related adverse events was higher with systematic treatment (17.4% vs. 7.2%; adjusted hazard ratio 2.57; 95% CI, 1.75 to 3.78). Serious adverse events were more common with systematic treatment.

Conclusion

Among severely immunosuppressed adults with HIV infection who had not previously received ART, systematic treatment for tuberculosis was not superior to test-guided treatment in reducing the rate of death or invasive bacterial disease over 24 or 48 weeks and was associated with more grade 3 or 4 adverse events.