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Outcomes of Nevirapine- and Efavirenz-Based Antiretroviral Therapy When Coadministered With Rifampicin-Based Antitubercular Therapy

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Context Rifampicin-based antitubercular therapy reduces the plasma concentrations of nevirapine and efavirenz. The virological consequences of these interactions are not well described.

Objective: To assess the effectiveness and tolerability of concomitant efavirenz- or nevirapine-based combination antiretroviral therapy and rifampicin-based antitubercular therapy.

Design, Setting, and Participants: Cohort analysis of prospectively collected routine clinical data in a community–based South African antiretroviral treatment program. Antiretroviral treatment-naive adults enrolled between May 2001 and June 2006 were included in the analysis, and were followed up until the end of 2006.

Interventions: Patients starting antiretroviral therapy with or without concurrent antitubercular therapy received either efavirenz or nevirapine at standard doses. Patients developing tuberculosis while taking antiretroviral therapy that included nevirapine were either changed to efavirenz or continued taking nevirapine.

Main Outcome Measures: Viral load of 400 copies/mL or more after 6, 12, and 18 months of antiretroviral therapy; time to the first viral load of 400 copies/mL or more; time to confirmed virological failure (2 consecutive values 5000 copies/mL); time to death; and time to treatment-limiting toxicity were assessed.

Results: The analysis included 2035 individuals who started antiretroviral therapy with efavirenz (1074 with concurrent tuberculosis) and 1935 with nevirapine (209 with concurrent tuberculosis). There were no differences in time to death or substitution of either antiretroviral drug for toxicity with and without concurrent tuberculosis. Patients starting nevirapine with concurrent tuberculosis were at a higher risk of elevated viral load most notably at 6 months (16.3%; 95% confidence interval [CI], 10.6%-23.5%) than those without tuberculosis (8.3%; 95% CI, 6.7%-10.0%; adjusted odds ratio [OR], 2.1; 95% CI, 1.2-3.4; and in the combined estimate, adjusted OR, 1.7; 95% CI, 1.2-2.6). In the time-to-event analysis of confirmed virological failure (2 consecutive values of 5000 copies/mL), patients starting nevirapine with concurrent tuberculosis developed virological failure sooner (adjusted hazard ratio [HR] 2.2; 95% CI, 1.3-3.7). There were no differences between patients starting efavirenz with and without concurrent tuberculosis (adjusted OR, 1.1; 95% CI, 0.8-1.5 [combined estimate] and adjusted HR, 1.1; 95% CI, 0.6-2.0, respectively). There was no difference in time to virological rebound in patients free of tuberculosis and those developing tuberculosis during follow-up while taking nevirapine (adjusted HR, 1.0; 95% CI, 0.5-2.0) or efavirenz (adjusted HR, 0.8; 95% CI, 0.4-1.7).

Conclusion: In this cohort study, virological outcomes were inferior when nevirapine-based antiretroviral therapy was commenced while taking antitubercular treatment (vs without concurrent tuberculosis) but comparable when starting efavirenz-based antiretroviral therapy (vs without concurrent tuberculosis) or when tuberculosis developed while taking established nevirapine- or efavirenz-based therapies.