

**Title:** Efficacy and Safety of Nevirapine versus Efavirenz when Combined in ART Regimens in HIV Infected Antiretroviral-Naïve Persons (The NNRTI Substudy of FIRST-CPCRA 058)

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**Background:** Although US guidelines recommend efavirenz (EFV) as preferred NNRTI, randomized comparisons of EFV and nevirapine (NVP) are limited and of short duration.

**Methods:** FIRST evaluated 3 strategies for initiating ART (PI+NRTI; NNRTI+NRTI; PI+NNRTI+NRTI). Patients specified whether the NNRTI would be determined by randomization (NVP or EFV) or by choice. For the randomized substudy, the primary endpoint was HIV RNA > 50 copies/mL after 8 months or death. Genotypic resistance testing was done at virologic failure (HIV RNA > 1,000 copies/mL after 4 months). Rates are per 100 person years.

**Results:** Among 927 patients randomized to an NNRTI-containing arm in FIRST, 228 consented to randomization in the NNRTI substudy (117 to NVP, 111 to EFV). Median age=37 years; 23% female; 79% non-white; median CD4+ 186 cells/mm<sup>3</sup>; median follow-up 5 years. Rates for the primary endpoint were 42.8 (NVP) and 41.2 (EFV); p=0.59. The percent of patients with HIV RNA < 50 copies/mL was similar throughout follow-up (p=0.24). Average increases in CD4+ were 153 (NVP) and 172 cells/mm<sup>3</sup> (EFV); p=0.3. Eighteen patients assigned NVP and 20 assigned EFV died: HR =1.18; p=0.62. Rates for progression of disease including death were 4.4 (NVP) and 7.4 (EFV); HR=1.67; 95% CI 0.98-2.83. Rates for any grade 4 adverse event were 10.2 (NVP) and 5.4 (EFV); HR=0.55; 95% CI 0.33-0.90. Rates for virologic failure with any drug resistance were 22.7 (NVP) and 13.3 (EFV); HR=0.60; 95% CI 0.39-0.93.

**Conclusions:** Virologic responses were comparable for patients randomly assigned NVP or EFV after median follow-up of 5 years; however, virologic failure on NVP was associated with more drug resistance. In the NVP arm there was a trend for lower rates of AIDS or death, however there were more adverse events. Larger, longer-term trials of initial ART regimens are needed to assess clinical outcomes with adequate power.