

Abstract category: B27 Initiation of therapy and first line regimens

Optional category: B21 Clinical trials - phase III/post-licensing

Abstract title:

Long-Term Clinical and Immunologic Outcomes Are Similar in HIV-Infected Persons Randomized to NNRTI vs PI vs NNRTI+PI-based Antiretroviral Regimens as Initial Therapy: Results of the CPCRA 058 FIRST Study

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Abstract text:

Background: Clinical outcomes data are lacking on the long-term consequences of initiating therapy with a PI, NNRTI, or both.

Methods: Between 1999 and 2002, 1397 treatment-naïve persons were randomized 1:1:1 to 1) PI+NRTIs, 2) NNRTI+NRTIs, or 3) PI+NNRTI+NRTI(s). Primary endpoints were a composite of AIDS events, death, and CD4+ cell count decline to <200 cells/mm³ (PI vs NNRTI comparison); and CD4+ cell count change after 32 months (3-class vs combined 2-class comparison).

Results: Median age was 38 years; 21% were female; 54% were black, 17% were Latino. Median CD4+ cell count was 163 cells/mm³. Median follow-up was 5 years. 302 persons developed an AIDS event or died; 188 died; 388 developed the composite clinical/CD4+ cell count endpoint. NNRTI vs PI hazard ratios (HRs) for the composite endpoint, AIDS or death, and virologic failure (VF) (HIV RNA >1000 copies/mL after 4 months) were 1.02 (95% CI: 0.79-1.31), 1.07 (0.80-1.41), and 0.66 (0.56-0.78), respectively. Mean increases in CD4+ cell counts after 32 months were 227 and 234 cells/mm³ for the combined 2-class and 3-class strategies (p=0.62), respectively. HRs (3-class vs combined 2-class) for AIDS or death and VF were 1.14 (95% CI: 0.91-1.45) and 0.87 (0.75-1.00), respectively. HRs (3-class vs combined 2-class) for AIDS or death and VF were similar for persons with baseline CD4+ cell counts <200 and >200 cells/mm³ (p=ns for interaction). Persons assigned the 3-class arm discontinued therapy due to toxicity more than those assigned the 2-class arms (HR=1.58, p<0.01).

Conclusions: NNRTI-based and PI-based strategies for initial therapy do not differ for a composite outcome based on CD4+ cell count decline, AIDS events, and death after a median follow-up of 5 years. The NNRTI strategy was superior virologically to the PI-based strategy. A 3-class strategy is not superior to a 2-class strategy for immunologic or clinical outcomes, and is associated with more drug toxicity.