To describe the early response to World Health Organization (WHO)-recommended nonnucleoside reverse transcriptase inhibitor (NNRTI)-based first-line highly active antiretroviral therapy (HAART) in HIV-1-infected Kenyan children unexposed to nevirapine. Observational prospective cohort. HIV-1 RNA level, CD4 lymphocyte count, weight for age z score, and height for age z score were measured before the initiation of HAART and every 3 to 6 months thereafter. Children received no nutritional supplements. Sixty-seven HIV-1-infected children were followed for a median of 9 months between August 2004 and November 2005. Forty-seven (70%) used zidovudine, lamivudine (3TC), and an NNRTI (nevirapine or efavirenz), whereas 25% used stavudine (d4T), 3TC, and an NNRTI. Nevirapine was used as the NNRTI by 46 (69%) children, and individual antiretroviral drug formulations were used by 63 (94%), with only 4 (6%) using a fixed-dose combination of d4T, 3TC, and nevirapine (Triomune; Cipla, Mumbai, India). In 52 children, the median height for age z score and weight for age z score rose from -2.54 to -2.17 (P<0.001) and from -2.30 to -1.67 (P=0.001), respectively, after 6 months of HAART. Hospitalization rates were significantly reduced after 6 months of HAART (17% vs. 58%; P<0.001). The median absolute CD4 count increased from 326 to 536 cells/μL (P<0.001), the median CD4 lymphocyte percentage rose from 5.8% before treatment to 15.4% (P<0.001), and the median viral load fell from 5.9 to 2.2 log10 copies/mL after 6 months of HAART (P<0.001). Among 43 infants, 47% and 67% achieved viral suppression to less than 100 copies/mL and 400 copies/mL, respectively, after 6 months of HAART. Good early clinical and virologic response to NNRTI-based HAART was observed in HIV-1-infected Kenyan children with advanced HIV-1 disease.