

Long-term Virologic Response and Genotypic Resistance Mutations in HIV-1 Infected Kenyan Children on Combination Antiretroviral Therapy.

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Abstract

Background: HIV-infected children may require the use of combination antiretroviral treatment (cART) into adulthood. However, regimens are limited to first- and second-line in many African settings. Therefore, understanding the long-term rate of virologic failure and drug resistance during prolonged antiretroviral treatment is important for establishing treatment strategies in African pediatric cohorts. Methods: Children ages 18 months to 12 years initiated first-line cART and were followed every 1-3 months, for up to 5.5 years. Treatment was switched to second-line based on clinical and immunologic criteria according to national guidelines. Virologic failure was determined retrospectively as defined by ≥ 2 viral loads >5000 copies/mL. Drug resistance was assessed during viral failure by population-based sequencing. Results: Among 100 children on first-line cART followed for a median 49 months, 34% experienced virologic failure. Twenty-three (68%) of the 34 children with viral failure had detectable resistance mutations, of whom 14 (61%) had multi-class resistance. Fourteen (14%) children were switched to second-line regimens and followed for a median of 28 months. Retrospective analysis revealed that virologic failure had occurred a median of 12 months prior to the switch to second-line. During prolonged first-line treatment in the presence of viral failure, additional resistance mutations accumulated, however, only 1 (7%) of 14 children had persistent viremia during second-line treatment. Discussion: Virologic suppression was maintained on first-line cART in two-thirds of HIV-infected children for up to 5 years. Switch to second-line based on clinical/immunologic criteria occurred ~ 1 year after viral failure, but the delay did not consistently compromise second-line treatment.