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Early Response to Highly Active Antiretroviral Therapy in HIV-1–Infected Kenyan Children

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Abstract

Objectives—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.

Design—Observational prospective cohort.

Methods—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.

Results—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

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Written informed consent was obtained from all study participants. Verbal assent was obtained from children between the ages of 7 and 12 years. This study received ethical approval from the Institutional Review Boards of the University of Washington and Kenyatta National Hospital.

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 $\log_{10}$ 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.

Conclusion—Good early clinical and virologic response to NNRTI-based HAARTwas observed in HIV-1–infected Kenyan children with advanced HIV-1 disease.

Keywords

antiretroviral; children; HIV-1; response

As programs providing highly active antiretroviral therapy (HAART) scale up in Africa, survival of HIV-1–infected children is expected to improve, based on what has been observed in Western settings.[1] In a recent study in Cote d'Ivoire, where the effects of protease inhibitor– or efavirenz-based HAART regimens were evaluated, 50% of children showed suppression of their HIV-1 plasma viral load to less than 250 copies/mL at 2 years.[2] In Kenya, there are an estimated 100,000 HIV-1–infected children, most of whom require antiretroviral therapy.[3] Most HIV-1–infected children in Kenya and other resource-poor settings present at an advanced stage of HIV disease, with marked immunosuppression because of delays in diagnosis and limited access to treatment.[2] This may potentially limit clinical benefits from HAART, given that in the Cote d'Ivoire study, children with a baseline CD4 lymphocyte percentage (CD4%) <5% had higher mortality than their counterparts with a CD4% >5%.[2]

The first-line HAART regimens recommended by the World Health Organization (WHO) and Kenyan national guidelines are nonnucleoside reverse transcriptase inhibitor (NNRTI) based.[4–6] For HIV-1–infected Kenyan children aged <3 years, nevirapine-containing HAART is recommended as first-line therapy, and for children aged >3 years, nevirapine or efavirenz is recommended. Nevirapine is first-line therapy, in part, because of its stability at room temperature in liquid form, favorable pharmacokinetic characteristics allowing for twice-daily dosing, lack of interaction with food, and relatively lower cost.[7] There is concern that nevirapine-based therapy may result in suboptimal viral suppression for children with extremely high viral loads, however.[7] The first-line regimens in resource-poor settings typically do not include protease inhibitors, for which there are extensive data showing reduction in mortality in Western settings.[1,4–6]

The virologic efficacy of nevirapine-containing triple therapy in early European and US studies ranged from 17% to 50%.[8–11] For example, in a study in the United Kingdom, only 17% of children on recommended doses of nevirapine achieved virologic suppression to <400 copies/mL at 96 weeks.[11] In these studies, children initiated HAART before the CD4% dropped to levels less than 10%, which is unlike most African children currently starting therapy. In a large US clinical trial, more than two thirds of the children had a CD4% ≥25% at enrollment, further highlighting the differences in timing of HAART initiation between the 2 settings.[12] More recently, however, better response to nevirapine-based HAART has been reported from the Thai national treatment program, with 71% of the children achieving viral suppression to less than 50 copies/mL at 72 weeks.[13] The Thai children had a median CD4% of 3% before the start of HAART.

In the pre-HAART era, African children experienced rapid and more aggressive HIV disease with higher mortality.[14] This observation, coupled with late presentation of children in advanced stages of HIV, underscores the need to define the efficacy of NNRTI-based and, in particular, nevirapine-containing HAART regimens in HIV-1–infected African children. We

undertook the present study to define the efficacy of first-line NNRTI-containing HAART in HIV-1–infected Kenyan children. This information should better inform treatment guidelines, with a view to maximize benefits from HAART as more HIV-infected children access therapy.

METHODS

Study Design and Subjects

We conducted a prospective cohort study at the Kenyatta National Hospital (KNH), beginning in August 2004, of HIV-1–infected Kenyan children aged 18 months to 12 years. Eligibility criteria included living in Nairobi, being antiretroviral drug naive, and presenting with advanced disease (WHO clinical stage 3–4) or having a CD4% <15% if in an earlier stage of disease. Children were recruited from the KNH pediatric wards and HIV Care Clinic and were enrolled after receiving written informed consent from their legal guardians.

Study Procedures

At baseline, medical information was obtained by interview and from hospital records. A complete physical examination was performed, and blood samples were collected for baseline hematologic assays, biochemical tests, CD4 cell profile, and plasma HIV-1 RNA viral load. Parents or legal guardians were counseled on the importance of drug adherence and on how to recognize common adverse drug reactions associated with antiretroviral drugs. The primary caregiver was identified as the person responsible for giving the child medications and bringing the child in for clinic appointments. Caregivers underwent 3 sessions of adherence counseling over a 2-week period before initiation of HAART, during which the importance of giving all antiretroviral drug doses was emphasized. Caregivers were advised to repeat dosing if the child vomited within 30 minutes of administering the antiretroviral drugs.

Antiretroviral Drugs

Antiretroviral therapy was initiated in accordance with Kenyan Ministry of Health guidelines.[5] The first-line anti-retroviral drug regimen consisted of zidovudine (AZT) and lamivudine (3TC) in combination with nevirapine or efavirenz. Nevirapine was prescribed for children aged less than 3 years, whereas older children received nevirapine or efavirenz. At the start of the study, some children were initiated on fixed-dose formulations of stavudine (d4T), 3TC, and nevirapine (Triomune; Cipla, Mumbai, India). Subsequently, individual antiretroviral drug formulations became available through the US President's Emergency Program for AIDS Relief (PEP-FAR), and most children used those. AZT (Retrovir; Glaxo-SmithKline, Parsippany, NJ) was given at a dose of 200 mg/m^2 twice daily, and 3TC (Epivir; GlaxoSmithKline) was given at a dose of 4 mg/m^2 twice daily. Nevirapine (Viramune; Boehringer Ingelheim, Ingelheim, Germany) was given at a lead dose of 120 mg/m^2 once daily for 2 weeks, which was subsequently increased to 200 mg/m^2 twice daily. Efavirenz (Stocrin; Merck, Whitehouse Station, NJ) was administered according to the manufacturer's insert based on the child's weight. Triple-nucleoside therapy, including abacavir (Ziagen; GlaxoSmith-Kline), was used for children less than 3 years of age who were on antituberculous treatment. Abacavir was administered at a dose of 8 mg/kg twice daily. AZT was replaced by d4T for children with a hemoglobin count less than 8 g/dL. d4T (Zerit; Bristol-Myers Squibb, Princeton, NJ) was given at a dose of 1 mg/kg twice daily.

Follow-Up

Children were followed at 2 weeks, at 1 month, and then at monthly intervals after HAART initiation for the first 9 months and once per quarter thereafter. At every appointment, a complete physical examination, including measurement of weight and height, was performed. Information regarding adherence, adverse drug effects, and intercurrent illness was obtained by interview. Follow-up hematologic and biochemical tests for liver function were performed 1 month after HAART initiation and quarterly thereafter. The CD4 cell profile was determined every 6 months, and the plasma HIV-1 RNA level was assessed quarterly. All children received daily cotrimoxazole prophylaxis against *Pneumocystis* pneumonia, according to the WHO/United Nations Program on HIV/AIDS (UNAIDS) recommendations.[15]

Adherence was assessed at each visit by self-report, where the caregiver was asked whether the child had missed any dose of antiretroviral drugs in the preceding 3 days and 2 weeks, respectively. If a child had missed any doses, further details were obtained as to the exact number of doses missed since the last clinic visit.

Clinical response to antiretroviral therapy was assessed by gain in weight and height and decreased frequency of hospitalization. Immunologic response was measured by change in $CD4^+$ T-lymphocyte count and CD4%, whereas virologic response was assessed by change in plasma HIV-1 RNA levels from baseline. Changes in total lymphocyte counts (TLCs) after HAART initiation were assessed as a potential surrogate marker for CD4 cell counts. An undetectable viral load was defined as <100 copies/mL. The analysis was repeated with a higher viral load cutoff of 400 copies/mL.

Laboratory Methods

HIV-1 was diagnosed using 2 rapid immunoassays, Determine (Abbott Laboratories, Abbott Park, IL) and Uni-Gold (Trinity Biotech, Dublin, Ireland), in a parallel testing algorithm. Plasma HIV-1 RNA assays were performed in Seattle using a transcription-mediated amplification (TMA) method developed by Gen-Probe (San Diego, CA).[16,17] This method has been tested and has shown high sensitivity for detection of Kenyan HIV-1 subtypes A, C, and D.[14] Personnel in Nairobi measured T-cell lymphocyte subsets using FACScan (Becton Dickinson, Franklin Lakes, NJ).

Statistical Methods

The primary outcomes of this study were changes from baseline in clinical, immunologic, and virologic parameters measured after initiating HAART. Height and weight measurements were converted into *z* scores using the nutrition module of Epi Info 3.2 (Centers for Disease Control and Prevention [CDC], Atlanta, GA). Body mass index *z* scores were also computed using Epi Info's nutrition module. This software sets a *z* score of 0 to correspond to the median score, whereas a score of −2 means 2 SDs less than the median. Reported hospitalization in the 6 months before initiating HAART was compared with that observed within the first 6 months of HAART by the McNemar test. We compared *z* scores, serum albumin levels, $CD4^+$ lymphocyte counts, CD4%, TLC, and plasma HIV-1 RNA levels before and after treatment using the Wilcoxon signed rank test. We also determined the proportion of children achieving undetectable plasma HIV-1 RNA (<100 copies/mL) after 3, 6, and 9 months of HAART, respectively. This analysis was repeated using a cutoff of 400 copies/mL to define undetectable viral load. Logistic regression was used to determine factors associated with viral suppression to less than 100 copies/mL after 9 months of HAART. Differences in baseline viral load and $CD4^+$ lymphocyte counts and CD4% between children who died versus those who survived were assessed using Mann-

Whitney *U* tests. STATA version 8 (Stata Corporation, College Station, TX) was used for the analyses.

RESULTS

Description of Study Subjects

Between August 2004 and November 2005, we enrolled 67 HIV-1–infected children, of whom 61 (91%) were followed for at least 3 months after HAART initiation (median = 9 months, range: 3–15 months). Six (9%) children died within 3 months of initiating HAART. Forty-six (69%) children were recruited as inpatients, whereas 21 (31%) were from outpatient settings. Only 1 child had received nevirapine for prevention of mother-to-child HIV-1 transmission. The median age at initiation of antiretroviral therapy was 4.4 years (range: 18 months to 12 years), and approximately half (51%) of the cohort was male. For 45 (67%) children, the biologic mother was the primary caregiver, whereas the biologic father was the primary caregiver for 11 (16%) of the children (Table 1).

Antiretroviral Therapy Regimens

Forty-seven (70%) children were initiated on a combination of AZT and 3TC and an NNRTI, whereas 17 (25%) were started on d4T and 3TC in combination with an NNRTI. Nevirapine was the most frequently prescribed NNRTI, and it was used for 46 (69%) children; efavirenz was prescribed for 18 (27%) children (Table 2). Two children on concomitant antituberculous therapy were started on triple-nucleoside therapy (AZT, 3TC, and abacavir and d4T, 3TC, and abacavir, respectively). The 1 child who had failed nevirapine perinatal prophylaxis was initiated on AZT, 3TC, and nelfinavir. Individual drug formulations were used by 63 (94%) children, whereas 4 (6%) used a fixed-dose combination of d4T, 3TC, and nevirapine (Triomune). These 4 children were later switched to individual drugs when they became available through the PEPFAR.

Response to HAART

Clinical Response—Anthropometric scores, serum albumin results, hospitalization history, and CD4 cell data were available at baseline and after 6 months for 52 children. After 6 months of HAART, there was a significant increase in the median height for age *z* score (−2.54 to −2.17; $P < 0.001$) and weight for age *z* score (−2.30 to −1.67; $P = 0.001$) (Table 3). In addition, serum albumin, a marker of macronutrient status, increased from a median of 33 g/L at baseline to 41 g/L after 6 months of HAART ($P < 0.001$).

In this subset of 52 children, 30 (58%) had been hospitalized at least once in the 6 months preceding initiation of HAART compared with only 9 (17%) in the first 6 months after HAART initiation ($P < 0.001$; see Table 3). Hospitalizations were attributable to infectious disease, including pneumonia, pulmonary tuberculosis, diarrhea, and severe failure to thrive.

Immunologic Response—In the 52 children with CD4 cell results available at baseline and after 6 months of HAART, the absolute CD4 cell count increased from a median of 326 cells/μL at baseline to 536 cells/μL at 6 months after HAART initiation ($P < 0.001$). Similarly, the median CD4% increased from 5.8% at baseline to 15.4% at 6 months after initiation of HAART ($P < 0.001$; see Table 3). Among children with follow-up to 15 months (n = 31), the median absolute CD4 count rose from 286 to 682 cells/μL ($P < 0.001$). For this group, the CD4% increased from 5.4% to 18.1% ($P < 0.001$). Overall, the CD4% increased by a median of 7.4% within 6 months of receiving HAART, and in the subset of 31 children with longer follow-up, the CD4% rose by a median of 11.3% (interquartile range [IQR]: 3.4–16.2) after 15 months of therapy.

Although we observed a modest increase in TLC after HAART initiation (median TLC from 3849 cells/mm^3 at baseline to 4025 cells/mm^3 after 6 months for 52 children), this change was not statistically significant ($P = 0.28$). After 15 months of HAART, the median TLC had risen to 4116 cells/mm^3 ($P = 0.59$ for change from baseline to 15 months).

Virologic Response—Viral load results were available at baseline and 3 months after HAART initiation for 50 children, at baseline and 6 months after HAART initiation for 43 children, and at baseline and 9 months after HAART initiation for 28 children. At baseline, children aged 3 years or less had a significantly higher viral load than those older than 3 years of age (median: 6.4 vs. 5.8 $\log_{10}$ copies/mL; $P = 0.007$; see Table 1).

Among children with a viral load available at baseline and 3 months (n = 50), the median plasma HIV-1 RNA load decreased from 6.0 $\log_{10}$ copies/mL at baseline to 2.5 $\log_{10}$ copies/mL 3 months after HAART initiation ($P < 0.001$). Viral load was suppressed to less than 100 copies/mL in 15 (30%) and to less than 400 copies/mL in 27 (54%) of these 50 children within 3 months of starting HAART (Table 4).

For children with a viral load available at baseline and 6 months (n = 43), the median viral load decreased from 5.9 $\log_{10}$ copies/mL at baseline to 2.2 $\log_{10}$ copies/mL at 6 months after HAART initiation ($P < 0.001$). Viral load was suppressed to less than 100 copies/mL in 20 (47%) and to less than 400 copies/mL in 29 (67%) of these 43 children within 6 months of starting HAART.

For the subset of children with a viral load available at baseline and 9 months after starting HAART (n = 28), the median viral load decreased from 5.9 $\log_{10}$ copies/mL at baseline to 2.1 $\log_{10}$ copies/mL after 9 months ($P < 0.001$). Eleven (39%) and 19 (68%) of the 28 children had viral suppression to less than 100 copies/mL and 400 copies/mL, respectively, 9 months after HAART initiation (see Table 4).

Correlates of Virologic Response—Children with a higher viral load at baseline were less likely to have a viral load less than 100 copies/mL after 9 months of HAART (odds ratio [OR] = 0.16 per $\log_{10}$-copies/mL increase in baseline viral load, 95% confidence interval [CI]: 0.03 to 0.80; $P = 0.025$; Table 5), and this effect was independent of the age of the child. There was a trend toward children whose parent(s) had undergone HIV testing before the child's enrollment being more likely to have a viral load less than 100 copies/mL after 9 months of HAART (60% vs. 20%, OR = 6.0, 95% CI: 0.93 to 38; $P = 0.06$). There was no association between self-reported adherence, baseline CD4%, or type of antiretroviral drug regimen used (nevirapine containing vs. efavirenz containing) and virologic response (see Table 5).

Mortality—Six (9%) children died after initiating antiretroviral therapy, all within the first 3 months of HAART. The median time to death was 57 days (range: 23–90 days). The children who died had a median age of 4.6 years, and 4 were male. The baseline HIV viral load was not significantly different between children who died early and those who survived beyond 3 months of treatment (median baseline viral load: 6.4 vs. 6.1 $\log_{10}$ copies/mL, respectively; $P = 0.23$). Although the baseline CD4 lymphocyte count and CD4% were lower in children who died early (median absolute CD4 count: 135 vs. 364 cells/μL, median CD4%: 5.1% vs. 6.3%), the differences did not reach statistical significance. There was also no significant difference in age or self-reported adherence between children who died and those who survived. The causes of death included cor pulmonale (n = 3), disseminated tuberculosis (n = 1), sepsis (n = 1), and severe pneumonia (n = 1). The 3 children who died of cor pulmonale had presented initially with predominantly right-sided congestive heart failure with severe digital clubbing. The child who died of suspected disseminated

tuberculosis presented with multiple abdominal masses and marked wasting and had radiographic evidence of hilar adenopathy. The child with sepsis presented with multiple sites of infection, including septic arthritis and skin abscesses, and had *Staphylococcus aureus* subspecies recovered from blood cultures.

Adherence to and Tolerance of Antiretroviral Drugs

Over the duration of follow-up, 43 (64%) caregivers reported never missing administering any antiretroviral drug dose, whereas 24 (36%) reported at least 1 missed dose. Of the 24 who reported a missed dose, 13 (54%) did so once, 8 (33%) reported missing between 2 and 5 doses, and 3 (13%) reported 6 or more missed doses since the last clinic visit.

Ten (15%) children changed at least 1 antiretroviral drug, of whom 7 did so because of severe adverse effects, 2 did so after treatment failure, and the remaining 1 did so to prevent drug interactions with the antituberculous drug rifampicin. Serious side effects included grade 2 to 3 nevirapine-associated rash in 4 children, AZT-associated anemia in 2 children, and abacavir hypersensitivity in 1 child. Minor side effects included grade 1 skin rash in 15 (22%) children and gastrointestinal effects, including nausea and vomiting, in 14 (21%) children. Of the children who experienced gastrointestinal effects, the symptoms subsided after 1 month of therapy in 11 (79%).

DISCUSSION

In this cohort of antiretroviral-naive HIV-1–infected Kenyan children with advanced immunosuppression, we observed good early clinical benefit and virologic response to the WHO first-line NNRTI-based HAART regimen. Seventy percent of the children in our cohort were treated with nevirapine-containing regimens, whose efficacy in African children is not well described.

The children experienced a good immunologic response, with a large proportion moving from the severe to moderate suppression category within the first 6 months of treatment.[4,18] The immune reconstitution was accompanied by a significant decline in hospitalization rates, which confirms the social and economic benefits of HAART that have been demonstrated in HIV-1–infected children receiving HAART in other settings.[19,20] By reducing the frequency of hospitalization, the cost to caregivers is lowered, given that they often have to pay out for pocket for such episodes.

We further observed significant early increases in anthropometric measures, including weight for age, height for age, and body mass index. Such positive impacts on a child's growth are key indicators of good response after initiation of antiretroviral therapy, as reported consistently across pediatric studies.[2,13,19] Our cohort consisted of children from poor settings, where malnutrition is highly prevalent. It is therefore possible that with nutritional supplementation, better weight gain may be achievable after HAART initiation in similar settings. Weight and height are simple clinical measurements that do not require costly sophisticated equipment and can be undertaken at all health facilities. Our findings strengthen the WHO's recommendation that where resources are limited, early response to HAART in children can be evaluated by regular weight measurements. As part of the scale-up of HAART to peripheral health facilities, children who show lack of early weight gain after initiation of therapy should be promptly referred for detailed evaluation and investigations in regional centers.

The virologic efficacy in our study (68% with HIV-1 RNA plasma viral load <400 copies/mL at 9 months after HAART initiation) is higher than that reported in children treated with nevirapine-containing HAART in early European and US studies, where efficacy ranged

from 25% to 50%.[7,11] In contrast, 71% of children on nevirapine-containing HAART in the Thai national program achieved viral suppression to less than 50 copies/mL after 72 weeks, which is higher than the 39% with levels less than 100 copies/mL at 9 months in our cohort.[13] Possible reasons for the superior efficacy in the Thai cohort may include longer duration of follow-up, higher levels of adherence, having older children with less viral burden at the start of therapy, or different viral strains.

Although other studies have found TLC to be a useful tool in monitoring the response to HAART in adults, our study did not demonstrate significant increases in the TLC in the short term.[21,22] This may be attributable, in part, to the small numbers of children and limited duration of follow-up.

The steady rise in serum albumin after initiation of HAART is evidence of macronutrient improvement experienced by the children. A recent study in Kenyan women found low serum albumin to be predictive of low selenium, which, in turn, has been associated with advanced HIV disease.[23,24]

All deaths in the study occurred early in the course of treatment. Of the 6 children who died, 3 succumbed to cor pulmonale resulting from recurrent chest infections in the pre-HAART period. It is likely that HAART was initiated too late in these children when the immune system had already been severely damaged or irreversible organ damage had occurred. There is growing evidence that children who start HAART with severe immunosuppression at a CD4% less than 5% may have higher mortality and may be unable to achieve optimal immune recovery, despite good virologic response in the long term.[2,25,26]

Ten percent of the children experienced serious side effects that necessitated withdrawal of the drugs; however, there was no drug-related mortality. This is a significant proportion of children and should raise concern for improved monitoring for serious toxicity as programs scale up in sub-Saharan Africa. Laboratory networks that transport samples collected from smaller peripheral sites to regional centers for assays and send results back should be encouraged.[2]

In summary, our study provides evidence that the NNRTI-based first-line antiretroviral regimen currently being scaled up for African children is highly efficacious and well tolerated in the short term. There is a need for long-term trials involving larger numbers to obtain further information on the prolonged use of HAART in African children.

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TABLE 1

Baseline Characteristics of HIV-1–Infected Children and Their Caregivers Before Initiating HAART

Characteristics	Median or Number (N = 67)	(IQR) or Percent
Child		
Age (y)	4.4	(2.4–6.0)
Male	34	51%
Clinical		
Weight for age *z* score	−2.45	(−4.3 to −1.54)
Weight for height *z* score	−1.34	(−2.85 to 0.09)
Height for age *z* score	−2.00	(−3.32 to −1.04)
Immunologic		
CD4 count, cells/μL	288	(101 to 560)
CD4%	6.2	(3.6 to 10.3)
CD4% <15%	55	82%
Virologic		
Log_{10} HIV-1 RNA copies/mL		
Age 18 months to 3 years	6.4	(6.0 to 6.6) *
Age >3 years	5.8	(5.3 to 6.3) *
Caregiver		
Age (y)	30	(26 to 37)
Education		
Primary	29	43%
Secondary	27	40%
College	7	10%
Married	42	63%
Relationship to child		
Mother	45	67%
Father	11	16%
Grandmother	6	10%
Other	5	7%

* Median viral load differs significantly between the 2 groups: $P = 0.007$.

TABLE 2

Antiretroviral Drug Regimens at Initiation

	Nevirapine	Efavirenz	Abacavir	Nelfinavir
AZT and 3TC	36	11	1[*]	1[†]
d4T and 3TC	10[‡]	7	1[*]	—

[*] Children had concomitant antituberculous treatment, including rifampicin.

[†] Child had been exposed to nevirapine as part of prevention of mother-to-child transmission.

[‡] Four of these used a fixed-dose formulation of Triomune (Cipla, Mumbai, India).

TABLE 3

Clinical and Immunologic Parameters Before and After 6 Months of HAART (n = 52*)

Characteristic	Before HAART	After HAART	*P*
	Median (IQR) or Number (%)		
Weight for age *z* score	−2.30 (−3.49 to −1.01)	−1.67 (−2.43 to −0.47)	0.001
Height for age *z* score	−2.54 (−3.56 to −1.44)	−2.17 (−2.86 to −1.13)	<0.001
Body mass index *z* score	−1.26 (−2.73 to −0.17)	−0.09 (−1.23 to 0.47)	0.01
Serum albumin, g/dL	33 (28 to 37)	41 (37 to 45)	<0.001
Hospitalized	30 (58%)	9 (17%)	<0.001
CD4 count, cells/μL	326 (86 to 540)	536 (273 to 841)	<0.001
CD4%	5.8 (3.1 to 9.7)	15.4 (9.8 to 21)	<0.001

*Subset of children who had all variables available at baseline and 6 months after HAART initiation.

TABLE 4

Virologic Response After Initiation of HAART

Time From HAART Initiation (mo)	No. Children*	Median HIV-1 RNA Viral Load (IQR)	VL <100 Copies/mL Number (%)	VL <400 Copies/mL Number (%)
0	65	6.1 (5.5 to 6.5)	1 (2)	1 (2)
3	50	2.5 (1.8 to 3.0)	15 (30)	27 (54)
6	43	2.2 (1.4 to 2.9)	20 (47)	29 (67)
9	28	2.1 (1.6 to 2.9)	11 (39)	19 (68)

*Attrition in numbers is attributable to loss through death and children still in follow-up. VL indicates HIV-1 RNA plasma viral load.

TABLE 5

Predictors of Viral Suppression to Less Than 100 Copies/mL at 9 Months of Treatment (n = 28)

Characteristic	OR (95% CI)	*P*
Univariate		
Female gender	1.6 (0.33 to 7.26)	0.58
Age (per year increase)	1.18 (0.83 to 1.69)	0.36
Plasma HIV-1 RNA (per $\log_{10}$ increase)	0.16 (0.03 to 0.80)	0.025
CD4% (per unit) *	0.99 (0.90 to 1.00)	0.32
Self-reported adherence problem	0.83 (0.17 to 4.01)	0.82
Nevirapine use (vs. efavirenz)	2.27 (0.36 to 14.5)	0.38
Parent tested for HIV before enrollment	6.0 (0.93 to 38)	0.06
Multivariate		
Plasma HIV-1 RNA (per $\log_{10}$ increase)	0.15 (0.03 to 0.87)	0.035 †

* Measured at baseline.

† Controlled for child's age.