Growth recovery among HIV-infected children randomized to lopinavir/ritonavir or NNRTI-based therapy

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Introduction

•HIV-infected African children suffer high rates of wasting and short stature.

•Growth generally improves with the initiation of antiretroviral therapy (ART), but data from two randomized trials have suggested poorer growth outcomes among children receiving lopinavir/ritonavir (LPV/r) vs. Nevirapine.[1,2]

•We compared the recovery of weight and height in a rural cohort of HIV-infected children randomized to initiate LPV/r- or non-nucleoside-reverse-transcription-inhibitor (NNRTI)-based ART.

Methods

•In the PROMOTE-pediatrics trial, HIV-infected children aged 2 months to 6 years were enrolled in Tororo, Uganda, and randomized to NNRTI- or LPV/r -based ART. [3,4]

•Children were seen monthly and received food supplementation if malnourished.

•Data from the 24 months following ART-initiation among ART-naive enrollees were included on a per-protocol basis.

•Change in gender-specific World Health Organization Z-scores for weight-for-age (WAZ) and height-for-age (HAZ) compared to baseline were evaluated using generalized linear repeated-measure models that adjusted for baseline Z-score score, socioeconomic status and confirmed virologic failure (consecutive HIV RNA > 400 copies/ml).

Results

• 129 ART-naïve children initiated ART, comprised of nevirapine (n=36) and efavirenz (n=29) in the NNRTI-arm.

• Median (IQR) follow-up times were 23.9 months (18.4, 23.9) for the LPV/r arm (n=64) and 23.8 months (17.5, 23.9) for the NNRTI arm

• The 96 week confirmed virologic failure rate was 26% (95%CI: 17%-39%) in the LPV/r arm and 28% (18%-41%) in the NNRTI-arm (Log-rank test p=0.8) in survival modeling[4].

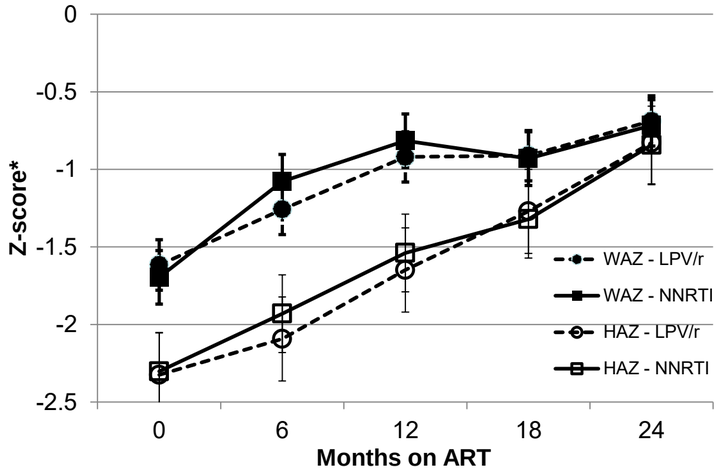
Table 1. Baseline characteristics

	LPV/r (n=64*)	NNRTI (n=65*)	P-value†
Age, years	3.2 (2.3 to 4.4)	3.1 (2.3 to 4.6)	0.97
Female	32 (30%)	35 (54%)	0.72
CD4 number, cells/µl	582 (397 to 969)	593 (389 to 788)	0.89
CD4 Percentage	17 (12 to 23)	16 (11 to 23)	0.77
HIV RNA, log(copies/ml)	5.3 (4.8 to 5.9)	5.3 (4.8 to 5.9)	0.75
WHO Stage			
I	39 (61%)	48 (74%)	
II	17 (27%)	11 (17%)	
III	2 (3%)	1 (2%)	
IV	6 (9%)	5 (8%)	0.82
WAZ	-1.5 (-2.4 to -0.6)	-1.2 (-2.3 to -0.6)	0.67
HAZ	-2.6 (-3.2 to -1.5)	-2.3 (-3.3 to -0.8)	0.59
WHZ	-0.2 (-1.1 to 0.6)	-0.1 (-0.9 to 0.5)	0.97

** Excludes the 2 children who withdrew or died before initiating study drugs. †Wilcoxon rank sum or Fisher's Exact test. Values are medians (interquartile range) or number (percentage); LPV/r, ritonavir-boosted lopinavir; NNRTI, non-nucleoside-reverse-transcriptase-inhibitor. WAZ: Weight-for-age Z-score; HAZ: Height-for-age Z-score; WHZ: Weight-for-height-for-age Z-score.*

- Height and weight of children in both arms improved steadily over 24 months following ART-initiation (Figure 1).
- The median (IQR) change in Z-scores among children who reached 24 months of follow-up on LPV/r (n= 45) vs NNRTI (n=40) were, respectively, WAZ: 0.47 (0.10, 1.62) vs 0.53 (0.03, 1.14) (p=0.59) and HAZ: median 1.55 (0.78, 1.86) vs 1.19 (0.62, 1.65) (p=0.23).
- In multivariate modeling, study arm (LPV/r vs. NNRTI) was not predictive of change in WAZ (beta: -0.02, 95%CI:-0.25, 0.20) or HAZ (beta: 0.05, 95%CI: -0.10, 0.19).

Figure 1. WAZ and HAZ after ART initiation



**Mean, with standard errors.*

Conclusions

- Our results suggest that as the use of LPV/r expands throughout Africa, HIV-infected children receiving LPV/r in similar settings can be expected to have comparable growth to children receiving NNRTI-based ART.
- That Z-scores remained below zero underscores the need for additional strategies to improve growth in HIV-infected African children.

References

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Acknowledgements

- *PROMOTE children, families and study team*
- *Makerere University - University of California, San Francisco Research Collaboration*
- *Infectious Disease Research Collaboration*
- *AbbVie (formerly Abbott Laboratories) for donation of lopinavir/ritonavir*
- *Eunice Kennedy Shriver National Institute of Child Health and Human Development (P01HD059454 and K23HD60459)*