eTable1: Multivariable associations with virologic failure using different predictor variables in main model and different failure definitions - Cox proportional hazards models stratified by site.

Failure definition	2 consecutive unsuppressed viral loads with the second being >1000 copies/ml		2 consecutive unsuppressed viral loads with the second being >1000 copies/ml in child with virologic response[§]		2 consecutive viral loads >10000 copies/ml		2 consecutive viral loads >400 copies/ml	
Characteristic at ART initiation	Adjusted HR (95% CI) Including WAZ and stage n=2356	p-value	Adjusted HR (95% CI) Excluding WAZ and stage n=3605	p-value	Adjusted HR (95% CI) Excluding WAZ and stage n=3605	p-value	Adjusted HR (95% CI) Excluding WAZ and stage n=3605	p-value
Age								
≥ 2 years	1	0.596[*]	1	0.676[*]	1	0.460[*]	1	0.714[*]
1 – 2 years	1.18 (0.74 – 1.86)		0.83 (0.53 - 1.30)		1.25 (0.75 - 2.09)		1.04 (0.73 - 1.50)	
< 1 year	0.96 (0.59 – 1.55)		0.96 (0.62 - 1.50)		1.39 (0.83 - 2.34)		1.15 (0.80 - 1.66)	
Female gender	0.88 (0.68 – 1.14)	0.337	0.81 (0.64 - 1.04)	0.098	0.89 (0.68 - 1.18)	0.426	0.91 (0.75 - 1.11)	0.361
Viral load > 1 million copies/ml	1.88 (1.37 – 2.58)	<0.001	2.12 (1.56 - 2.87)	<0.001	1.84 (1.31 - 2.59)	<0.001	1.70 (1.32 - 2.18)	<0.001
Severe immunosupression	1.49 (0.99 – 2.25)	0.058	1.36 (0.95 - 1.95)	0.097	1.49 (0.98 - 2.25)	0.059	1.24 (0.94 - 1.65)	0.134
WHO stage 3 or 4 (vs 1 or 2)	1.36 (0.97 - 1.90)	0.075						
Weight-for-age z-score <-3	0.89 (0.64 - 1.23)	0.47						
Third drug in regimen								
Efavirenz	1		1		1		1	
Nevirapine	1.45 (0.79 - 2.64)	0.228	2.09 (1.23 - 3.54)	0.006	1.66 (0.91 - 3.02)	0.101	1.88 (1.20 - 2.94)	0.006
Lopinavir/ritonavir	1.10 (0.69 - 1.73)	0.695	1.16 (0.77 - 1.74)	0.475	0.73 (0.45 - 1.20)	0.218	1.08 (0.77 - 1.51)	0.648
Ritonavir alone	2.54 (1.48 - 4.37)	0.001	2.35 (1.43 - 3.88)	0.001	1.92 (1.09 - 3.39)	0.023	2.26 (1.50 - 3.41)	<0.001
PMTCT exposure								
Unexposed /unknown	1		1		1		1	
Exposed	1.33 (0.93 - 1.91)	0.118	1.18 (0.80 - 1.75)	0.396	1.36 (0.89 - 2.07)	0.152	1.30 (0.95 - 1.77)	0.096

[*]p-values derived from Wald's test

[§]> 1 $\log_{10}$ reduction in viral load from baseline during first 15 months on ART

Title: Virologic failure and second-line antiretroviral therapy in children in South Africa - The IeDEA Southern Africa Collaboration

Abstract

Background: With expanding pediatric antiretroviral therapy (ART) access, children will begin to experience treatment failure and require second-line therapy. We evaluated the probability and determinants of virologic failure and switching in children in South Africa.

Methods: Pooled analysis of routine individual data from children who initiated ART in 7 South African treatment programs with 6-monthly viral load and CD4 monitoring produced Kaplan-Meier estimates of probability of virologic failure (two consecutive unsuppressed viral loads with the second being >1,000 copies/ml, after ≥24 weeks of therapy) and switch to second-line. Cox proportional hazards models stratified by program were used to determine predictors of these outcomes.

Results: The 3-year probability of virologic failure among 5485 children was 19.3% (95%CI: 17.6-21.1). Use of nevirapine or ritonavir alone in the initial regimen (compared to efavirenz), and exposure to prevention of mother to child transmission regimens were independently associated with failure (adjusted hazard ratios (95%CI): 1.77(1.11-2.83), 2.39(1.57-3.64) and 1.40(1.02-1.92) respectively). Among 252 children with ≥1 year follow-up after failure, 38% were switched to second-line. Median (IQR) months between failure and switch was 5.7(2.9-11.0).

Conclusion: Triple ART based on nevirapine or ritonavir as a single protease inhibitor appears to be associated with a higher risk of virologic failure. A low proportion of virologically failing children were switched.

Keywords: antiretroviral therapy, virologic failure, children; second-line therapy, resource-limited setting