Mortality Across Two ART Trials Enrolling at ≤200 verses ≤350 CD4 cells/uL in Kenya

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Background

- In 2011, Kenyan HIV treatment guidelines changed from initiating ART at a CD4 of ≤200 to ≤350 cells/uL. Guidelines were changes again to initiating ART at ≤ 500 cells/ul in June of 2014.
- We compared 6-month mortality in 2 research cohorts, one enrolled before and one after the 2011 ART initiation guidelines changed.
- Early mortality following HAART initiation may be unaffected by ARVs since early deaths are often caused by already advanced illness due to co-infection or to immune reconstitution syndrome.
- We hypothesized that following the new guidelines to initiate HAART at higher CD4 counts, 6-month mortality following ART initiation would be lower in a cohort of patients initiating HAART in 2013 vs. 2006 for clinical trials.

Methods

- **Study Population:** HIV seropositive adults enrolled in 2 clinical trials at the Coptic Hope Center, in Nairobi Kenya with similar enrollment criteria.
  - 2006: Drug Adherence Intervention
  - 2013: Drug Resistance Testing Intervention
- **Inclusion Criteria:** ART-naïve HIV seropositive adults enrolled in a clinical trial.
- **Follow-up**: Patients were followed during monthly visits for 18 months in 2006 and 15 months in 2013. Missed visits were investigated to determine if the participant had died or were unable/unwilling to participate using standardized procedures across both studies.
- **Statistical Analysis**
  - Subjects who enrolled after Aug 4 2014 and those who withdrew or died prior to HAART initiation were omitted from the analysis.
  - Subjects who were loss to follow-up were censored at the last time-point they were known to be alive. Subjects were administratively censored at 180 days if they had not died or were loss to follow-up prior to that time point.
  - A t-test was used to compare mean baseline CD4 between cohorts.
  - Cox proportional hazards regression was used to calculate hazard ratios (HR) comparing mortality between the study cohorts using time from enrollment to death within 6 months.

Acknowledgements

- We thank the participants in the different studies and the health care team members at the Coptic Hope Center, Nairobi, Kenya
- These studies were supported by the National Institutes of Health (NIH)

Results

Table 1. Participant baseline characteristics by study cohort

Variable[§]	2006 Adherence Study (N=400)	2013 Resistance Study (N=515)
Age (years)*	37 (8); 36 (31, 42)	39 (10); 38 (33, 46)
Female*	265 (66%)	228 (44%)
Married or Attached	205 (51%)	273 (53%)
Education (years)	11 (4); 11 (8, 13)	11 (4), 12 (8, 14)
Unemployed*	129 (32%)	216 (42%)
Flush toilet*	183 (46%)	311 (61%)
# of persons living in house*	4 (2); 4 (2, 5)	4 (2); 3 (2, 5)
Travel time to clinic (hours)*	0.93 (0.96); 0.67 (0.5, 1)	1.45 (2.41); 1 (0.67, 2)
Age of sexual debut (years)*	18 (3); 18 (16, 20)	18 (3); 18 (16, 20)
Lifetime sexual partners	6 (10); 4 (2, 7)	6 (20); 3 (2, 5)
Ever exchange money for sex*	40 (10%)	29 (6%)
CD4 count*	125 (82); 116 (61, 183)	194 (165); 180 (77, 280)

[§]For continuous variables, the mean (standard deviation), and median (inter quartile range) are presented. For binary variables the N (%) are presented. *Indicates p-value <0.05. For continuous variables, a t-test assuming unequal variance was performed, and for binary variables, a chi^2 test was performed, comparing the 2013 and 2006 cohorts.

Figure 1. Kaplan-Meier Survival Estimates: 6-Month Mortality by Cohort

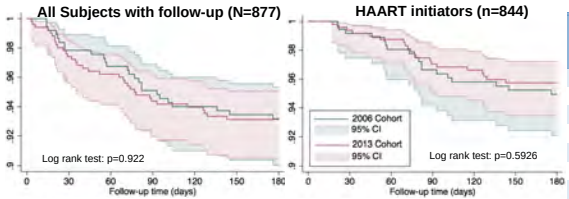

Table 2. Frequency of death and loss or withdraw from study (LTFU) within 6 months by cohort and HAART initiation status

Status at 6 months	2006 cohort (N=400)			2013 cohort (N=515)		
	Initiators	Non-initiators	Total	Initiators	Non-initiators	Total
LTFU	13 (4%)	29 (76%)	42 (11%)	40 (8%)	17 (52%)	57 (11%)
Death	18 (5%)	8 (21%)	26 (7%)	20 (4%)	14 (42%)	34 (7%)
Living	331 (91%)	1 (3%)	332 (83%)	422 (88%)	2 (6%)	424 (82%)
Total	362 (100%)	38 (100%)	400 (100%)	482 (100%	33 (100%)	515 (100%)

Figure 2. Kaplan-Meier survival estimates: 6-month mortality by cohort and enrollment CD4 (all subjects with follow-up)

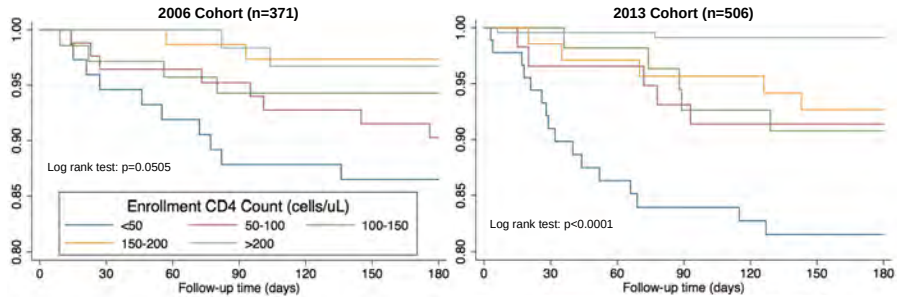

Table 3. Distribution of CD4 count and mortality by study cohort

CD4 Count (cells/ul)	All Subjects				Mortality Incidence	
	2006		2013		2006	2013
Category	N (%)	N (%) died	N (%)	N (%) died	N (%)	N (%)
<50	82 (21%)	10 (12%)	92 (18%)	16 (17%)	10 (2.5%)	16 (3.1%)
50-99	92 (23%)	8 (9%)	58 (11%)	5 (9%)	8 (2%)	5 (1%)
100-149	72 (18%)	4 (6%)	56 (11%)	5 (9%)	4 (1%)	5 (1%)
150-199	83 (21%)	2 (2%)	70 (14%)	5 (7%)	2 (0.5%)	5 (1%)
>200	69 (1%)	2 (3%)	237 (46%)	2 (1%)	2 (0.5%)	2 (0.4%)
Missing CD4	2 (0.5%)	0 (0%)	2 (0.4%)	1 (50%)	0 (0%)	1 (0.2%)
Total	400 (100%)	26 (7%)	515 (100%)	34 (7%)	400 (100%)	515 (100%)

Table 4. Hazard ratios (HR) for 6-month mortality

Model Adjustments (at baseline)	2013 vs. 2006 HR (95% CI); p-value	
	All subjects with FU time	HAART initiators
Unadjusted	0.97 (0.58, 1.62); 0922	0.84 (0.44, 1.59); 0.593
Age & Sex	0.99 (0.58, 1.68); 0.965	0.85 (0.44, 1.65); 0.634
Time to Clinic	0.97 (0.58, 1.62); 0.910	0.86 (0.45, 1.65); 0.650
Unemployed	0.96 (0.57, 1.59); 0.862	0.84 (0.44, 1.59); 0.596
CD4 count	1.23 (0.73, 2.06); 0.440	1.11 (0.58, 2.13) 0.756

Summary

- Higher CD4 was associated with lower mortality within 6 months in both cohorts.
- More subjects enrolled with higher CD4 count in 2013.
- There was no statistically significant difference in mortality risk within 6 months between the cohorts.
- 2013 had lower 6 month mortality than 2006 among those who initiated HAART (not significant).
- 3% fewer subjects subjects enrolled with a CD4 count <50 cells/uL in 2013 (18%) than in 2006 (21%).
- Mortality within 6 months among those with CD4 <50cells/uL was greater in 2013 (17%) than 2006 (12%).

Conclusions

- With implementation of guidelines to initiate ART at a higher CD4 count (from ≤200 to ≤350 cells/uL), the mean CD4 count increased among those accessing care to initiate ART (125 cells/uL in 2006 vs. 194 cells/uL in 2013).
- Despite new guidelines, many participants initiated ART with dangerously low CD4 counts <50 cells/uL. Earlier HIV diagnosis and rapid linkage to care is necessary to achieve survival gains from new ART guidelines.