EFFECT OF SELENIUM SUPPLEMENTATION ON CD4 T-CELL RECOVERY AND MORBIDITY AMONG HIV-POSITIVE INDIVIDUALS IN RWANDA: A RANDOMIZED CONTROL TRIAL

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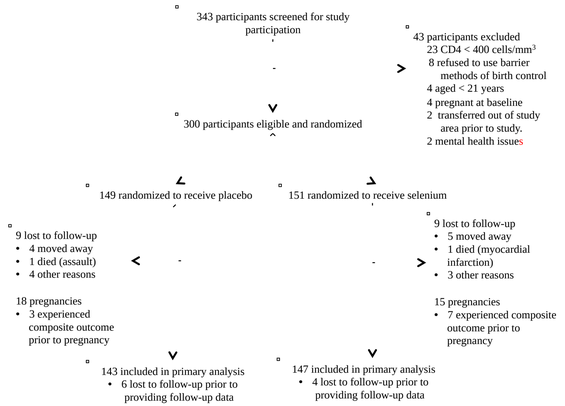
Background

- HIV infection compromises the nutritional status of infected individuals and poor nutritional status can accelerate progression of the disease.[1]
- Selenium deficiencies, indicated by low plasma selenium concentrations, have been documented among HIV-positive individuals, particularly in areas of the world with low selenium levels in the soil as in much of Sub-Saharan Africa. However evidence of the effect of selenium supplementation on viral load and CD4 outcomes from randomized clinical trials is limited
- Three RCTs documenting the effect of daily selenium supplementation have produced mixed results.[2-4] Additional evidence from other settings and populations is required to more accurately determine the effect of selenium supplementation on HIV progression in HIV-infected individuals.
- Our RCT aimed to examine the effect of selenium supplementation on CD4 T-cell counts, viral suppression and quality of life among ART-naïve individuals in Rwanda

Methods

- We conducted a patient and provider blinded, randomized placebo-controlled clinical trial among 300 ART-naïve individuals in Rwanda.
- Participants were recruited from three health facilities and eligibility criteria included:
  - HIV-infected adults (21 years of age or older);
  - Being not yet ART-eligible;
  - Having a CD4 T-cell count between 400 and 650 cells/mm^3;
  - Being willing to practice barrier methods of birth control at all times;
  - Not being pregnant and;
  - Being able to provide informed consent.
- Participants were randomized using a simple randomized block design to receive either 200 µg selenium or an identical placebo taken daily for 24 months (Figure 1)
- The study ran for 24 months and the primary outcome measure was change in CD4 T-cell count at 6,12,18 and 24 months
- For analyses of the primary outcome, patients were censored after ART initiation.

Figure 1. Randomization flow chart



Methods (continued)

- Secondary outcomes included: time to viral suppression; a composite of CD4 T-cell depletion to 350 cells/mm^3(as confirmed by 2 consecutive measures), or start of ART, or the emergence of a documented CDC-defined AIDS-defining illness; mortality; and adverse events.
- Baseline demographic and clinical characteristics were tabulated and compared using Fisher's Exact test for dichotomous outcomes and Wilcoxon's rank-sum test for continuous outcomes.
- All analyses were based on the intention-to-treat (ITT) approach using the randomized treatment assignment.
- For the primary outcome, we used linear regression with generalized estimating equations (GEE) for the repeated measures.
- Both time-to-event analyses (Cox proportional hazards regression and Kaplan Meier curves) and simpler contingency table analyses were used to determine whether selenium supplementation could delay the initiation of ART.
- As self reported adherence was measured over time, we used it as a time-varying covariate.

Results

- Three-hundred participants, randomized (151 to the selenium arm and 149 to placebo) had an average CD4 T-cell count of 555 cells/mm^3
- Seventeen participants were lost to follow-up, one non-AIDS death occurred in each group and 23 (15 in the selenium arm and 8 in placebo) women were time censored due to pregnancy and resulting ART initiation.
- **Table 1** summarizes baseline characteristics of both treatment arms.

Table 1 A and B: Baseline characteristics

Variable	*Values*	*Total*	*Active*	*Placebo*	*p-value*
Gender	Male	98	44 (29.1%)	54 (36.2%)	0.151
	Female	202	107 (70.9%)	95 (63.8%)	
Marital status	Married or living with partner	180	90 (60.8%)	90 (60.4%)	0.916
	Single	26	15 (10.1%)	11 (7.4%)	
	Widowed	32	15 (10.1%)	17 (11.4%)	
	Separated	41	19 (12.8%)	22 (14.8%)	
	Divorced	18	9 (6.1%)	9 (6%)	
Employment	No	132	65 (43.3%)	67 (45.3%)	0.585
	Yes	165	84 (56%)	81 (54.7%)	
	Refused	1	1 (0.7%)	0 (0%)	
Has had sex in past month	No	110	50 (33.3%)	60 (40.3%)	0.214
	Yes	189	100 (66.7%)	89 (59.7%)	
Number of partners in past 30 days	N.A. (Skipped)	110	50 (33.3%)	60 (40.5%)	0.390
	1	185	98 (65.3%)	87 (58.8%)	
	2	3	2 (1.3%)	1 (0.7%)	
Condom use in past 30 days	N.A. (Skipped)	110	50 (33.3%)	60 (40.5%)	0.233
	Always	104	59 (39.3%)	45 (30.4%)	
	Sometimes	30	12 (8%)	18 (12.2%)	
	Never	54	29 (19.3%)	25 (16.9%)	

Variable	*N1*	*Active*	*N2*	*Placebo*	*P-value*
AGE	151	33.0 (28.0-39.0)	149	35.0 (28.0-41.0)	0.418
BMI_BASE	132	21.5 (19.8-23.7)	134	21.6 (20.0-24.3)	0.379
LVLbase	136	3.8 (3.0-4.5)	132	3.9 (3.3-4.4)	0.324
CD4_BASE	151	552.0 (470.0-636.0)	149	527.0 (465.0-610.0)	0.126

- The rate of CD4 depletion was reduced by 43.8% among patients receiving selenium supplementation (95% Confidence Interval [95% CI]: 7.8-79.8%)
- Results of the GEE linear regression are summarized in **Table 2**.
- The differences in CD4 depletion rates are shown in **Figure 2A**.

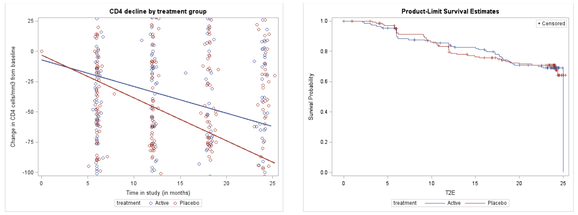
Results (continued)

- Overall, we found no treatment effect for the composite outcome (hazard ratio: 1.00, 95% CI: 0.66-1.54) or viral suppression (Odds Ratio [OR]: 1.18, 95% CI: 0.71-1.94), but the trial was underpowered for the composite outcome. The trial was powered based on the assumption of a more rapid decline into ART eligibility.
- No significant differences between treatment and placebo arms were noted across all adverse events

Table 2: Linear regression for CD4 decline

Variable	Average CD4 Change (95% Confidence Interval)	P-value
Treatment		
Active vs. Placebo	-4.37 (-13.78, 5.04)	0.363
Time (per month)	-3.97 (-4.91, -3.03)	<0.001
Time adjustment		
Active vs. Placebo	1.74 (0.31, 3.17)	0.017

Figure 2. Rate of CD4 T-cell count decline across treatment groups And Kaplan-Meier plot of time to composite outcome results



Conclusion

- Among ART-naïve HIV-positive adults in Rwanda, 24-month selenium supplementation is safe and significantly decreased the rate of immune decline (as measured by rate of CD4 T-cell depletion)
- Evidence with respect to delayed ART initiation was more limited and may warrant more research

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