Is CD4 Monitoring Needed Among Ugandan Clients Achieving a Virologic and Immunologic Response to Treatment

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Background

•Immunologic monitoring with CD4 cell counts every 3-6 months is commonly performed for individuals receiving antiretroviral therapy (ART)

•In the setting of an immunologic and virologic response to ART (CD4>200 cells/ul and HIV viral load (VL) <400 copies/ml) it is unclear whether ongoing CD4 monitoring is necessary

Objective

•To investigate the proportion of clients who achieved a virologic and immunologic response to ART who had a subsequent decline in CD4 (<200 cells/ul) despite virologic suppression

Methods

•Clients receiving ART from Rakai Health Sciences Program (RHSP) in southwestern Uganda were eligible for this analysis if the satisfied the following criteria:

- Achieved CD4>200 cells/ul and HIV VL<400 copies/ml
- Had at least 3 sets of CD4/VL measurements within a 390 day period (defined as a sequence)

•Clients were monitored routinely with CD4 and VL every 6 months until January 2011 when VL monitoring was performed annually after the first year on ART

•Kaplan Meier survival curves were generated to compare the probability of maintaining as CD4≥200 cells/ul, within a single sequence within different CD4 count strata at initiation of a sequence (ie. 200-249, 250-299, 300-349, and ≥350 cells/ul

•A Cox proportional hazards model was used to identify factors associated with a CD4 decline

Results

•A total of 1553 clients were receiving first-line ART and included in this analysis

•Among these, 1482 (95.4%) had at least one sequence of CD4/VL measurements, while 71 (4.6%) had more than one sequence

•On average, clients acquired a sequence after 8.3 months on ART (6.9-14.2)

•The median (IQR) duration between each paired CD4/VL tests was 169 days (169-183)

Table 1: Baseline characteristics of patients receiving antiretroviral therapy

Characteristic	Value
Gender	
Female, n (%)	**1052(67.7)**
Male, n (%)	**501(32.3)**
Age	
Mean (SD)	**35.5(8.3)**
≤19 years, n (%)	**11(0.7)**
20-29 years, n (%)	**367(23.6)**
30-39 years, n (%)	**723(46.6)**
40-49 years, n (%)	**363(23.4)**
>49 years, n (%)	**89(5.7)**
First CD4 Cell Count at start of the first sequence	
Median (IQR)	**335(265-428)**
101-250, n (%)	**296(19.1)**
251-350, n (%)	**556(35.8)**
351-550, n (%)	**542(34.9)**
>550, n (%)	**159(10.2)**
WHO Clinical Stage	
1, n (%)	**523(33.7)**
2, n (%)	**570(36.7)**
3, n (%)	**330(21.3)**
4, n (%)	**121(7.8)**
Unknown, n (%)	**9 (0.6)**
ART Start Regimens	
AZT/3TC/NVP, n (%)	**660(42.5%)**
AZT/3TC/EFV, n (%)	**438(28.2%)**
D4T/3TC/NVP, n (%)	**306(19.7%)**
D4T/3TC/EFV, n (%)	**137(8.8%)**
TDF/3TC/NVP, n (%)	**2(0.1%)**
TDF/3TC/EFV, n (%)	**3(0.2%)**
Other, n (%)	**6(0.4%)**

Table 2: Distribution by patient and sequence analysis based on initial CD4 while under continuous viral suppression

Initial CD4 in Sequence*	All	200-249	250-299	300-349	≥350
Per-client analysis	**1553**	**294**	**299**	**254**	**706**
CD4 count maintained at ≥200 cells/µl during viral suppression (%)	1510(97.2)	275(93.5)	286(95.7)	245(96.5)	704(99.7)
CD4 count declines (%)	43(2.8)	19(6.5)	13(4.3)	9(3.5)	2(0.3)

* Sequence defined as ≥3 sequential CD4 and VL measurements occurring within 390 days

Results

•Of 43 clients who developed declines, 24 had an additional CD4 during later follow-up and 20/24 (83%) achieved a CD4>200 on their next visit

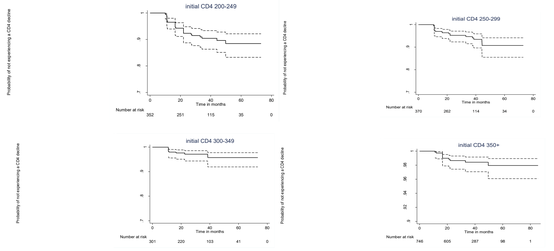
•No opportunistic infections occurred among clients experiencing a CD4 decline

•Multivariate analysis of predictors of CD4 decline revealed the following:

- lower CD4 at sequence initiation (AHR 4.3 (95% CI 2.1,9.0) CD4 200-249 versus ≥350
- A 50-cell increase in baseline CD4 was associated with a reduced risk of CD4 decline, AHR 0.8 (95% CI 0.71, 0.96)

treatment regimen and gender were not associated with CD4 declines

Figure 1: Kaplan Meier curves showing per-patient analysis of probability of maintaining a CD4 ≥200cells/µl, within a single sequence



Conclusions

•We found the risk of experiencing a CD4 decline to be very low among individuals who achieved an immunologic (CD4 ≥200 cells/ul) and virologic (VL<400 copies/ml response to treatment and among those who experienced a decline, the majority were transient in nature

•As access to VL monitoring expands in resource limited settings, decreasing the The frequency of CD4 monitoring among virally suppressed clients may reduce costs

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