



## Background

- WHO guidelines recommend switching to AZT/3TC (plus a third drug) in patients who fail a first-line regimen including TDF/3TC
- Due to the toxicity of AZT and demonstrated efficacy of nucleoside reverse transcriptase inhibitors (NRTIs) in spite of genotypic resistance in recent studies, TDF/3TC is often continued in second-line ART in resource-poor settings
- However, recent anonymized data from a randomly selected subset of patients failing efavirenz (EFV)/TDF/3TC (n=90) at GHESKIO, in Port-au-Prince, Haiti, found high rates of NRTI resistance; nearly 30% of patients had the K65R mutation and nearly all of these patients had co-existing M184V or other NRTI mutations. In contrast, 93% of this cohort was sensitive to AZT according to the Stanford database.

### Study Objectives:

1. To describe the characteristics of patients who failed EFV/TDF/3TC and started on a second-line regimen including TDF/3TC or AZT/3TC, in combination with either lopinavir or atazanavir boosted with ritonavir (boosted protease inhibitor [bPI])
2. To evaluate the impact of staying on TDF/3TC vs switching to AZT/3TC on retention, viral load, and adherence

## Methods

- **Study design and population:** Retrospective cohort study that included all patients at GHESKIO who failed first-line EFV/TDF/3TC and switched to a second-line regimen that included TDF/3TC or AZT/3TC, in combination with a bPI. Patients who had received any other ART medications were excluded.
- **Outcomes:** Patients who had at least one visit  $\geq 6$  months after initiating second-line ART were considered retained in care. Among patients retained on second-line treatment, 6-month adherence was measured using pharmacy refill data (number of days ART was dispensed, divided by 183 days). Undetectable viral load (VL) was defined as VL <200 copies/ml.
- **Statistical analysis:** Comparisons between patients who continued TDF vs. switched to AZT were analyzed using Chi Square test (or Fisher's exact test as appropriate) for categorical variables and Wilcoxon rank sum test for continuous variables. Logistic regression models adjusting for baseline characteristics including age, year of second-line ART initiation, gender, education, and civil status were used to estimate odds ratios (OR) and 95% confidence intervals (CI)

## Results

### Patient Characteristics (Table 1)

- Of 1,017 patients at GHESKIO who met the study criteria, 733 (72.1%) continued TDF/3TC in combination with a bPI for second-line treatment [TDF/3TC group], and 284 (27.9%) switched to AZT/3TC/bPI [AZT/3TC group]

Table 1. Characteristics at Second-Line ART Initiation

	Overall N=1,107	TDF/3TC N=733	AZT/3TC N=284	P-value
<b>Demographic characteristics</b>				
Age (years) - median [IQR]	40.8 [34.0, 50.2]	41.0 [33.9, 50.2]	40.4 [34.5, 49.1]	0.722
Gender, n (%)				0.048*
Male	508 (50.0)	352 (48.0)	156 (54.9)	
Female	509 (50.0)	381 (52.0)	128 (45.1)	
<b>Education level</b>				
None or primary only	563 (55.4)	400 (54.6)	163 (57.4)	0.416
Secondary and above	421 (41.4)	302 (41.2)	119 (41.9)	0.839
Missing	33 (3.2)	31 (4.2)	2 (0.7)	
<b>Civil status</b>				
Single	237 (23.3)	184 (25.1)	53 (18.7)	0.029*
Married	104 (10.2)	74 (10.1)	30 (10.6)	0.825
Formerly married	229 (22.5)	158 (21.6)	71 (25.0)	0.238
Unmarried couple	414 (40.7)	286 (39.0)	128 (45.1)	0.078
Missing	33 (3.2)	31 (4.2)	2 (0.7)	
<b>Treatment characteristics</b>				
Year second-line ART started				<0.001*
2012-2014	130 (12.8)	69 (9.4)	61 (21.5)	
2015-2016	371 (36.5)	237 (32.3)	134 (47.2)	
2017-2018	516 (50.7)	427 (58.3)	89 (31.3)	

\* for p-value <0.05



Samuel Pierre  
spierre@gheskio.org

Poster presentation number P058

## Results (continued)

### Treatment Outcomes (Table 2)

- The median [IQR] follow-up time from second-line ART initiation to last visit or database closure was 14.6 [10.3, 27.2] months for TDF/3TC and 24.4 [13.4, 39.0] months for AZT/3TC group
- Overall, 550 (75.0%) in TDF/3TC and 193 (68.0%) in AZT/3TC group remained in care on second-line ART
- Due to differential follow-up times, outcomes are reported at 6 months after second-line ART initiation (Table 2).

Table 2. Treatment outcomes

	Overall N=1,107	TDF/3TC N=733	AZT/3TC N=284	P-value
<b>Patient status 6 months after 2nd-line ART initiation (%)</b>				
Loss to follow-up	102 (10.0)	68 (9.3)	34 (12.0)	0.199
Died	20 (2.0)	15 (2.0)	5 (1.8)	0.768
Remained in care on 2nd-line ART	895 (88.0)	650 (88.7)	245 (86.3)	0.289
No viral load information	329 (36.8)	264 (40.6)	65 (26.5)	<0.001*
At least one VL test $\geq 6$ months after 2 <sup>nd</sup> -line ART initiation	566 (63.2)	386 (59.4)	180 (73.5)	<0.001*
<200 copies/ml	278 (49.1)	204 (52.8)	74 (41.1)	0.009*
$\geq 200$ copies/ml	288 (50.9)	182 (47.2)	106 (58.9)	0.009*
Time from starting 2nd-line ART to first VL test (months), median [IQR]	11.3 [8.0, 17.2]	10.9 [7.6, 16.3]	13.3 [9.1, 20.2]	<0.001*
<b>6-month adherence (among patients retained in care)</b>				
$\geq 90\%$	n=740 454 (61.4)	n=547 351 (64.2)	n=193 103 (53.4)	0.008*
<90%	286 (38.6)	196 (35.8)	90 (46.6)	

\* for p-value <0.05

### Multivariable Analyses:

- **Predictors of retention in care for at least 6 months of second-line ART:**
  - At least secondary education (vs. primary/none): OR 1.55 [95% CI: 1.01, 2.37]
- **Predictors of 6-month adherence  $\geq 90\%$  on second-line ART:**
  - Remaining on TDF/3TC (vs. AZT/3TC): OR 1.62 [95% CI: 1.14, 2.29]
  - Married or unmarried couple (vs. single): OR 1.66 [95% CI: 1.12, 2.48]
  - Formerly married (vs. single): OR 1.69 [95% CI: 1.01, 2.82]
- **Predictors of first viral load test <200 copies/ml:**
  - Remaining on TDF/3TC (vs. AZT/3TC): OR 1.77 [95% CI: 1.21, 2.57]
  - Married or unmarried couple (vs. single): OR 1.90 [95% CI: 1.21, 2.98]
  - Formerly married (vs. single): OR 1.84 [95% CI: 1.04, 3.25]
  - 2016-2018 year of initiation (vs. 2012-2015): OR 0.68 [95% CI: 0.46, 1.00]
  - At least secondary education (vs. primary/none): OR 1.61 [95% CI: 1.12, 2.33]
- **Among those with adherence  $\geq 90\%$ , predictors of VL <200 copies/ml were:**
  - Education (at least secondary vs. primary/none): OR 2.02 [95% CI: 1.19, 3.43]

## Limitations

- Only 59.4% of patients in the TDF/3TC and 73.5% in the AZT/3TC group had viral load information available
- Adherence could be over-estimated if patients picked up ART at the pharmacy but didn't take their medications
- Due to short follow-up time in the TDF/3TC group, outcomes are reported for only 6 months on second-line ART

## Discussion and Conclusion

- The proportion of patients with viral suppression on second-line ART is low in Haiti, even among patients with high adherence by pharmacy refill data
- Though rates of viral suppression are sub-optimal regardless of the NRTI backbone, our data suggest that switching to AZT/3TC is associated with worse outcomes than remaining on TDF/3TC
- New regimens for second-line ART are needed in settings such as Haiti, with high rates of NRTI resistance and no access to ART resistance testing for patients initiating second-line ART

## Acknowledgments

We thank all patients and staff at the GHESKIO HIV care and treatment clinics who participated in this project and thank Dr. Gustavo Reyes-Terán, Dr. Claudia García-Morales, and Dr. Santiago Avila Ríos from the Centre for Research in Infectious Diseases of the National Institute of Respiratory Diseases in Mexico City for their help.