ACTG 5381: Virologic and Resistance Outcomes After Switch to TLD for Failing 1st or 2nd Line ART

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BACKGROUND

Most countries recommend tenofovir-lamivudine-dolutegravir (TLD) for individuals starting antiretroviral therapy (ART) or switching from suppressive 1st-line NNRTI- or 2nd-line PI-based ART, but national guidelines vary about switching to TLD when not suppressed on ART.

METHODS

- Adults and adolescents (>10 years) switching from 1st-line NNRTI-based (**Cohort 1**) or 2nd-line PI-based (**Cohort 2**) ART with HIV-1 RNA >1000 c/mL were enrolled in the ACTG A5381 prospective cohort study.
- Plasma HIV-1 RNA was measured at study entry and every six months for up to 36 months. For participants with HIV-1 RNA >1000 c/mL at six months, population-based genotyping was performed on the study entry and six month samples.
- At the 6-month visit, the proportion with HIV-1 RNA ≤1000 c/mL and the proportion with new DTG resistance mutations were estimated among those still on TLD. Exact 95% confidence intervals (CI) were calculated using the Clopper-Pearson method.
- A case-control study (unsuppressed vs. suppressed) evaluated tenofovir diphosphate (TFV-DP) concentrations in dried blood spots.

RESULTS

Table 1. Participant Characteristics

	Cohort 1: switched from failing 1st-line NNRTI-based ART (N=44)	Cohort 2: switched from failing 2nd-line PI-based ART (N=173)
Female sex, n (%)	34 (77%)	98 (57%)
Gender identity, n (%)		
Cisgender	43 (98%)	163 (94%)
Not reported	1 (2%)	10 (6%)
Age (years), median (q1, q3)	33 (24, 41)	41 (27, 49)
Country, n (%)		
Haiti	2 (5%)	80 (46%)
Kenya	19 (43%)	27 (16%)
Malawi	2 (5%)	13 (8%)
South Africa	3 (7%)	9 (5%)
Uganda	15 (34%)	44 (25%)
Zimbabwe	3 (7%)	0 (0%)
HIV-1 RNA (log_{10} c/mL), median (q1, q3)	4.0 (3.7, 4.6)	4.2 (3.6, 4.6)
CD4 count (cells/mm^3), median (q1, q3)	306 (173, 419)	262 (134, 370)
Total years on ART, median (q1, q3)	5.5 (3.1, 9.2)	5.4 (2.8, 8.9)

Infrequent emergence of DTG mutations and lower TFV-DP concentrations in unsuppressed vs. suppressed after switch to TLD suggest suboptimal viral suppression is due to incomplete adherence.

Table 2. Proportion of participants with HIV-1 RNA ≤1000 and ≤200 c/mL at months 6, 12, and 24.

		Cohort 1: switched from failing 1st-line NNRTI-based ART (N=44)		Cohort 2: switched from failing 2nd-line PI-based ART (N=173)	
		% (n / N on TLD with RNA results)	Exact 95% CI	% (n / N on TLD with RNA results)	Exact 95% CI
HIV-1 RNA ≤1000 c/mL	6 months	88% (37/42)	74%, 96%	72% (118/165)	64%, 78%
	12 months	88% (30/34)	73%, 97%	74% (104/140)	66%, 81%
	24 months	76% (16/21)	53%, 92%	70% (45/64)	58%, 81%
HIV-1 RNA ≤200 c/mL	6 months	83% (35/42)	69%, 93%	67% (110/165)	59%, 74%
	12 months	88% (30/34)	73%, 97%	65% (91/140)	57%, 73%
	24 months	76% (16/21)	53%, 92%	61% (39/64)	48%, 73%

Figure 1. Proportion of participants with HIV-1 RNA ≤1000 c/mL at each study visit. Vertical bars represent exact 95% confidence intervals.

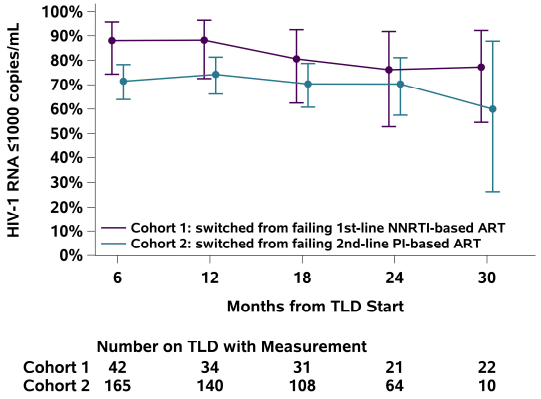
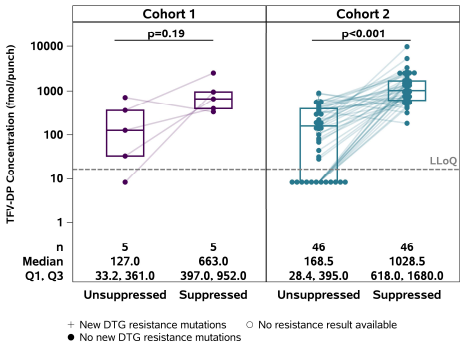


Table 3. Proportion of participants with HIV-1 RNA >1000 c/mL and new DTG resistance mutations at the 6-month visit. Two participants who switched from failing 2nd-line PI-based ART had new DTG mutations (G118R and R263K).

	Cohort 1: switched from failing 1st-line NNRTI-based ART (N=44)		Cohort 2: switched from failing 2nd-line PI-based ART (N=173)	
	% (n / N on TLD with integrase resistance results)	Exact 95% CI	% (n / N on TLD with integrase resistance results)	Exact 95% CI
HIV-1 RNA >1000 c/mL with new DTG mutations	0% (0/42)	0%, 8%	1% (2/163)	0%, 4%

Figure 2. TFV-DP concentrations at the 6-month visit compared between the case and control groups using a Wilcoxon signed rank test. Concentrations below the lower limit of quantification (LLoQ) of the assay (16.6 fmol/3mm punch) were imputed as half of the LLoQ. Boxes represent median (q1, q3).



CONCLUSIONS

- Participants who switched to TLD from failing 1st or 2nd-line ART had improved but suboptimal (<90%) viral suppression that did not improve over time.
- Infrequent emergence of DTG mutations and lower TFV-DP concentrations in unsuppressed vs. suppressed participants suggest that incomplete adherence to TLD was the major mechanism for failure to suppress viremia.
- Lower suppression rates were observed among participants switching from failing 2nd-line PI-based ART vs. failing 1st-line NNRTI-based ART. This is consistent with the possibility that individuals who have failed two prior ARV regimens vs. one prior ARV regimen might have greater adherence challenges.

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