HIV drug resistance by next-generation sequencing after transition to TLD in Uganda and South Africa

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Background

- Studies have identified an increased risk of dolutegravir (DTG) resistance in people with a history of nucleos(t)ide reverse transcriptase inhibitor (NRTI) resistance after transition to tenofovir/lamivudine/dolutegravir (TLD).

Objective: To determine frequency of DTG resistance and impact of NRTI resistance on the emergence of DTG resistance minority variants

Methods

- **Study design**: Prospective observational cohort
- **Sample Size and Setting**: 999 participants
  - Mbarara, Uganda (n=500)
  - KwaZulu-Natal, South Africa (n=499)
- **Study population**: Adults (≥18 years of age) transitioning from NNRTI-based ART to TLD as first-line therapy
- Next generation sequencing was performed on specimens with VL> 500 copies/mL at enrollment, 24-, and 48-weeks
- We examined the frequency of HIV-1 resistance mutations at 2%, 5%, and 20% thresholds.
- Genotypic susceptibility scores (GSS) were calculated using the Stanford algorithm, and resistance was defined as GSS ≤0.5 (low, intermediate, or high-level resistance).

Table 1. Study population characteristics

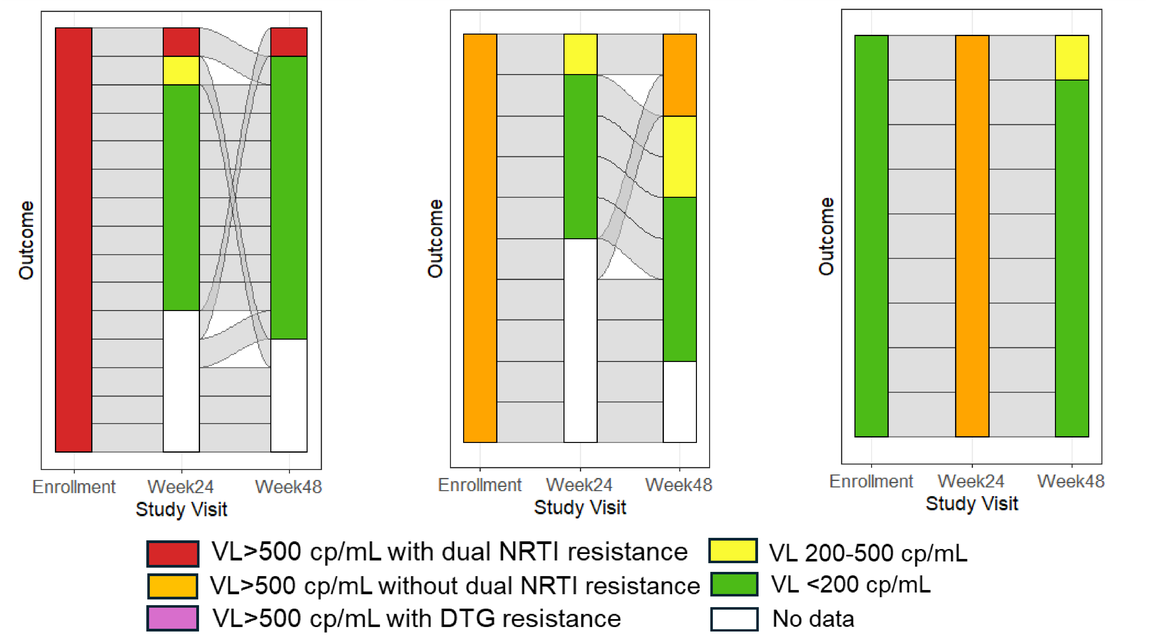
Characteristic	Total Cohort (N=999)
Age (years), median (IQR)	44 (36-51)
Female, n (%)	604 (61%)
Years on ART, median (IQR)	7 (5-11)

Among ~1,000 people who transitioned from NNRTI ART to TLD in public sector clinics in Uganda and South Africa, **resistance to TDF and 3TC at transition was not associated with emergent DTG resistance, including minority variants.**

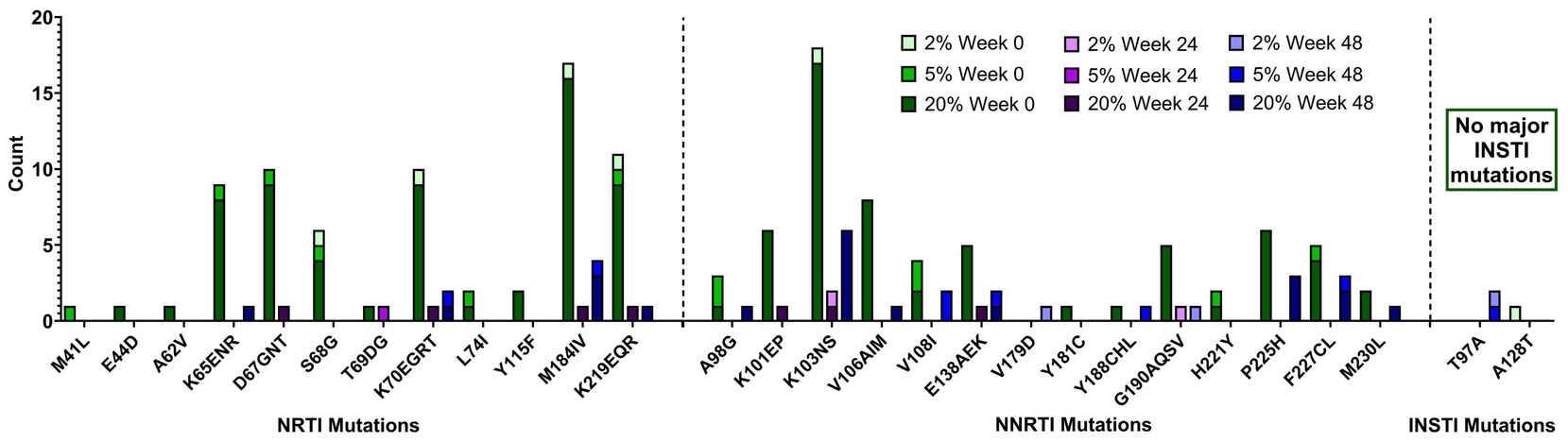
Dual NRTI resistance at enrollment (n=15)

Viremia without dual NRTI resistance at enrollment (n=10)

Emergent viremia without resistance at Week 24 (n=9)



HIV-1 Resistance mutations at 2%, 5%, and 20% thresholds of detection



Conclusions

- No study participants, including those with resistance to TDF and 3TC at the time of TLD transition or at 24 weeks, had DTG resistance (based on resistance mutations detected at ≥2% threshold), after one year on TLD.
- Among individuals who transitioned to TLD with dual NRTI resistance, 67% achieved viral suppression at 48 weeks. This compares to 90% viral suppression among those who were suppressed at the time of TLD transition (p=0.015).

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