Discordance of HIV Drug Resistance and Clinical Outcomes in Kenyan Youth with Perinatal HIV

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BACKGROUND

- HIV drug resistance testing informs regimen design, yet discordance between resistance findings and clinical outcomes challenges interpretation algorithms.
- This is especially critical for vulnerable populations, such as adolescents and young adults (youth) with perinatally acquired HIV in resource-limited settings.

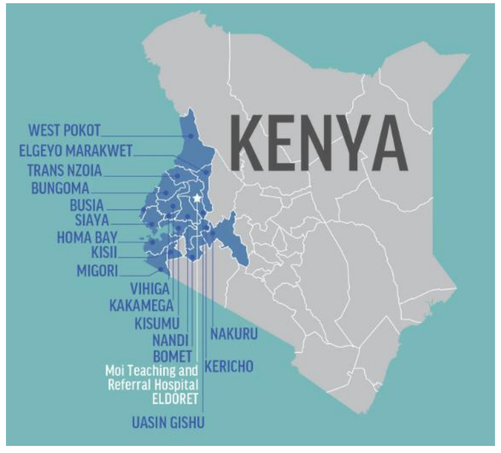
OBJECTIVE

- To characterize discordance between HIV drug resistance and clinical outcomes.

METHODS

- We followed Kenyan youth with perinatal HIV at the Academic Model Providing Access to Healthcare (AMPATH; Fig. 1) every 6 months for 4 years, 2020-2025.
- We defined **2 clinical scenarios for Discordance** (Fig. 2):
  1. **Resistance** to ≥ 1 drug in regimen **and** subsequent viral load (VL) **suppression** (VL<200 copies/mL)
  2. **No resistance** to all drugs in regimen **and** subsequent **viral failure** (VL≥200 copies/mL)
- Genotyping was attempted for all viremic youth.
- Enrollment into the nested cohort studies was at the 1st visit with VL≥200 copies/mL and a genotype.
- Resistance was defined as Stanford Database level ≥3 to one or more of the current regimen drugs.
- Time to discordance was evaluated with pooled logistic regression for discrete event-time data, with robust standard errors.
- Associations with discordance were evaluated for age, sex, years on antiretroviral therapy, dolutegravir (DTG)-based regimen, number of drugs with resistance, adherence (by a validated questionnaire; score 0-6; higher is worse) and VL.

Figure 1. Study Setting



Discordance between HIV drug resistance and clinical outcomes is common in Kenyan youth, highlighting limitations of resistance interpretation algorithms. Additional mechanisms, beyond conventional resistance and adherence, may shape outcomes, underscoring the need for further research to guide care in the DTG era.

RESULTS

- 444 youth were enrolled, of whom 71 fit into clinical scenario 1 and 111 into clinical scenario 2 (Table 1).
- Discordances were seen in 29% (128/444) of youth; 79% (128/163) of those with at least one genotype.
- **Discordance in Clinical Scenario 1 (Resistance + Suppression):**
  - Overall, of 71 who had ≥3 level resistance to their regimen, 66 (93%) had subsequent VL<200; on DTG: 27/28 (96%); not on DTG: 39/43 (91%); 37% reported perfect adherence.
  - Discordance was in 54% by month 6 and 96% by study end (Fig. 3).
  - Discordance occurred sooner with worse baseline adherence and lower VL (Table 2).
- **Discordance in Clinical Scenario 2 (No Resistance + Viral Failure):**
  - Overall, of 111 who had no ≥3 level resistance to their regimen, 82 (74%) had subsequent VL>200; on DTG: 66/93 (71%); not on DTG: 16/18 (89%); 35% reported perfect adherence.
  - Discordance was in 48% by month 6 and 88% by study end (Fig. 3).
  - Discordance occurred sooner with higher VL (Table 2).

Figure 2: Examples of Clinical Scenarios *

*Clinical Scenario 1 ***

Visit	VL	Predicted Resistance		
		TDF	3TC	DTG
M00	0			
M06	0			
M12	0			
M18	0			
M24	0			
M30	0			
M36	154			
M42	274	3	5	4
M48	0			

Time

Clinical Scenario 2

Visit	VL	Predicted Resistance		
		TDF	3TC	DTG
M00	0			
M06	0			
M12	1666	1	1	1
M18	621	1	1	1
M24	2342	1	1	1
M30	7064	1	1	1
M36	7710	1	1	1
M42	9308			

* Red boxes: enrollment visit; green boxes: discordant visit. Predicted resistance = Stanford level.
** Resistance at the M42 visit: INSTI R263K; NRTI D67N, K70R, M184V, K219Q.

Figure 3: Discordance over time by clinical scenario

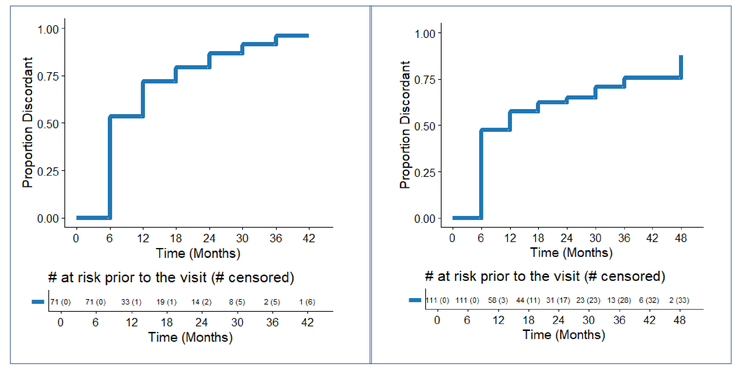


Table 1. Characteristics of Study Participants by Clinical Scenario

Characteristic	Clinical Scenario 1: (N = 71)	Clinical Scenario 2: (N = 111)
Male	28 (39%)	61 (55%)
Age *	17 (16, 20)	18 (17, 21)
Duration of Antiretroviral Therapy (Years) *	12.8 (11.4, 15.1)	12.6 (11.0, 14.4)
Non-Adherence Questionnaire Score *	1 (0, 3)	1 (0, 3)
Viral Load (copies/mL) *	1,953 (759, 7,115)	5,908 (1,244, 47,204)
Number of antiretrovirals with 3+ resistance		
1	37 (52%)	—
2	25 (35%)	—
3	9 (13%)	—
Antiretroviral regimen		
DTG-based	34 (48%)	93 (84%)
PI-based	34 (48%)	18 (16%)
NNRTI-based	3 (4%)	0 (0%)
Medication switch during follow-up		
Any	14 (20%)	7 (6.3%)
To DTG	12 (17%)	3 (2.7%)
Recent CD4 Count; Cells/μL *	803 (536, 1,056)	742 (498, 959)
Recent CD4% *	27 (19, 36)	30 (19, 37)

* Median (IQR).

Table 2. Associations with Discordance by Clinical Scenario

Variable	Clinical Scenario 1		Clinical Scenario 2	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Log Viral Load	0.50 (0.22, 1.13)	0.096	1.38 (1.10, 1.74)	0.006
Non-Adherence Questionnaire	1.57 (1.00, 2.45)	0.048	0.83 (0.58, 1.17)	0.283
On DTG	3.11 (0.37, 25.9)	0.293	0.89 (0.15, 5.39)	0.895
Resistance to 2–3 antiretrovirals vs 1	1.20 (0.06, 25.8)	0.909	—	—
Age (years)	1.05 (0.79, 1.39)	0.735	1.05 (0.88, 1.24)	0.607
Male	1.52 (0.32, 7.20)	0.601	1.70 (0.62, 4.63)	0.299
Years on Antiretroviral Therapy	0.92 (0.48, 1.75)	0.794	0.87 (0.67, 1.12)	0.288

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