Low Rate of Resistance to Dolutegravir in Adolescents Living With HIV-1 in West and Central Africa

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BACKGROUND

Achieving good adherence to ART and sustaining viral suppression remain challenging in adolescents with HIV-1 (AHIV). However, since the large-scale rollout of DTG-based ART in pediatrics, few data are available on ART outcomes in AHIV, particularly in West and Central Africa.

We sought to evaluate the rate of virological failure (VF) and HIV-1 drug resistance in AHIV living in Benin, Cameroon, Ivory Coast and Senegal.

METHODS

Within the frame of the EVA network, the CABRILADO study was conducted among consenting AHIV, aged 12-17 years and followed in 8 pediatric centers. Clinical and sociodemographic parameters were collected. Plasma HIV-1 RNA was measured and sequencing of RT, protease and integrase was performed on samples with pVL ≥1000 cp/mL. HIV drug-resistant viruses (HIV-DR) were identified and interpreted using the ANRS-MIE v35 algorithm.

Encouraging rate of viral suppression (82% at a 200 cp/mL threshold).

In AHIV with VF while on DTG:

* HIV-DR to INSTIs in 12.7% (n=7)
* Resistance to DTG in 4.2% (n=3)

RESULTS

All 637 enrolled AHIV were on ART. Most of them (93.7%) received DTG (as part of the first-line regimen in 14% of cases).

VF at 1000 cp/mL, 200 cp/mL and 50 cp/mL thresholds:

- in 12%, 18% and 29% of AHIV, respectively (Table 2).
- in 12%, 18% and 28% of those receiving DTG, respectively.

Factors associated with VF (≥50 cp/mL): prior VF, being raised by a guardian and stunting (Table 3).

	Benin (n=170)	Cameroon (n=190)	Ivory Coast (n=137)	Senegal (n=140)	Total (n=637)
Age (years) (median, IQR)	15 (14-17)	16 (14-17)	15 (14-17)	16 (14-17)	16 (14-17)
Female gender (n, %)	101 (59.4)	106 (55.8)	60 (43.5)	66 (47.1)	333 (52.3)
Nutritional status	62 (36.5)	16 (8.4)	19 (13.9%)	27 (19.3)	124 (19.5)
stunting (n, %)					
Person(s) in charge of the AHIV's raising					
Parent(s) (n, %)	120 (70.6)	136 (71.6)	96 (70.1)	85 (60.7)	437 (68.6)
Guardian(s) (n, %)	50 (29.4)	54 (28.4)	41 (29.9)	55 (39.3)	200 (31.4)
Mode of HIV acquisition					
Vertical (n, %)	155 (91.2)	187 (98.4)	132 (96.4)	131 (93.6)	605 (95.0)
Other/unknown (n, %)	15 (8.8)	3 (1.6)	5 (3.6)	9 (6.4)	32 (5.0)
Age at HIV diagnosis (years) (median, IQR)	6 (2–11)	3 (1–7)	4 (2–6)	5 (2–9)	4 (2–8)
History of virological failure					
Yes (n, %)	52 (30.6)	57 (30.0)	18 (13.1)	39 (27.9)	166 (26.1)
No (n, %)	118 (69.4)	133 (70.0)	119 (86.9)	101 (72.1)	471 (73.9)
Anchor drug included in the current ART regimen					
EFV (n, %)	0 (0.0)	0 (0.0)	1 (0.7%)	4 (2.9)	5 (0.8)
DTG (n, %)	**167 (98.2)**	**158 (83.2)**	**136 (99.3)**	**136 (97.1)**	**597 (93.7)**
ATV/r (n, %)	3 (1.8)	32 (16.8)	0 (0.0)	0 (0.0)	35 (5.5)

Table 1. Clinical and sociodemographic characteristics of 637 adolescents

	Benin (n=170)	Cameroon (n=190)	Ivory Coast (n=137)	Senegal (n=140)	Total (n=637)
Current HIV viral load (cp/mL)					
<50 (n, %)	117 (68.8)	134 (70.5)	92 (67.3)	111 (79.3)	454 (71.3)
50-199 (n, %)	23 (13.5)	20 (10.5)	17 (12.4)	7 (5.0)	67 (10.5)
200-999 (n, %)	11 (6.5)	15 (7.9)	10 (7.3)	4 (2.9)	40 (6.3)
≥1000 (n, %)	19 (11.2)	21 (11.1)	18 (13.1)	18 (12.9)	76 (11.9)
HIV-DR in AHIV with pVL≥1000 cp/ml					
HIV-DR to NRTIs (n %)	7 (36.8)	2 (18.2)	2 (18.2)	8 (50.0)	19 (33.3)
HIV-DR to NNRTIs (n %)	8 (42.1)	4 (36.4)	4 (36.4)	4 (25.0)	20 (35.1)
HIV-DR to PIs (n %)	1 (5.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.9)
HIV-DR to INSTIs (n %)	**3 (15.8)**	**0 (0.0)**	**0 (0.0)**	**4 (25.0)**	**7 (12.5)**
Missing data, n	0	1	7	0	8

Table 2. Results of plasma HIV-RNA and prevalence of HIV-DR in AHIV with pVL ≥1000 cp/mL

Variables	OR	95% CI	P-value
Country			0.020
Benin	-	-	
Cameroon	1.10	[0.67 – 1.81]	
Ivory Coast	1.51	[0.89 – 2.56]	
Senegal	0.61	[0.35 – 1.07]	
Gender			0.9
Female	-	-	
Male	1.03	0.71, 1.49	
Age	1.00	0.89, 1.13	>0.9
History of sexual intercourse with a girl/boy-friend			0.11
No	-	-	
Yes	1.85	0.87, 3.91	
History of VF (HIV-1 RNA ≥400 cp/ml measured ≥ 6 months after the 1st ART initiation)			**<0.001**
No	-	-	
Yes	**2.84**	**1.92, 4.21**	
Main person responsible for raising the AHIV			**0.017**
Mother	-	-	
Father	0.73	0.42, 1.23	
Guardian	**1.53**	**1.03, 2.28**	
Growth (height-for-age)			**0.043**
Normal	-	-	
Stunting	**1.61**	**1.01, 2.55**	

Table 3. Multivariable logistic regression of factors associated with VF (pVL ≥50 cp/mL)

HIV-DR to INSTIs:

- in **12.5%** of available sequences in 76 AHIV with pVL ≥1000 cp/ml
- in **12.7%** of available sequences in 71 AHIV with pVL ≥1000 cp/ml ***while on DTG***

HIV-DR to DTG:

- in **3.9%** of available sequences in 76 AHIV with pVL ≥1000 cp/ml
- in **4.2%** of available sequences in 71 AHIV with pVL ≥1000 cp/ml ***while on DTG***

In AHIV receiving DTG

DTG-resistant viruses in 3 cases:

- R263K DRM in a AHIV on 1st-line DTG
- E138K+G140A+S147G+Q148R DRM in a pretreated AHIV
- E138K+Q148K DRM in a pre-treated AHIV.

Other HIV-DR to INSTIs in 4 cases: T97A (n=3) and E157Q DRM (n=1)

Functional DTG monotherapy in 1 case: M41L+D67N+K70R+L74I+M184V+T215F+K219Q DRM in the RT gene.

CONCLUSIONS

In this large West and Central African multi-country cohort, viral suppression of AHIV appears encouraging.

The prevalence of DTG-resistant viruses remains low in AHIV with VF while receiving DTG. In order to mitigate further risks of functional monotherapy, continuous monitoring of HIV drug resistance is required in this vulnerable population requiring lifelong ART.

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