



High Prevalence of Transmitted Drug Resistance in HIV-1-infected Antiretroviral-naïve Patients from Conakry, Guinea-Conakry



M Diakite¹, C Charpentier^{2,6}, P Bellecave³, M Cisse⁴, G Peytavin^{5,6}, B Djoudalbaye⁶, L Pizzarro⁶, C Katlama^{6,7}, F Huber⁶, B Masquelier^{3,6}, D Descamps^{2,6}

1-Laboratoire de Virologie, CHU Donka, Conakry, Guinée-Conakry; 2-Laboratoire de Virologie, Hôpital Bichat-Claude Bernard, Paris, France; 3-Laboratoire de Virologie, CHU Bordeaux, France; 4-Service de Dermatologie, CHU de Donka, Conakry, Guinée-Conakry, 5-Laboratoire de Pharmacologie Hôpital Bichat-Claude Bernard, Paris, France; 6-Solthis, Paris, France; 7-Service des Maladies Infectieuses et Tropicales, Hôpital Pitié-Salpêtrière, Paris, France

E-mail: diane.descamps@bch.aphp.fr

BACKGROUND

To assess the prevalence of transmitted drug resistance and to study viral tropism in HIV-1 infected antiretroviral naïve patients from Conakry (Guinea-Conakry).

PATIENTS AND METHODS

- ✓ 100 newly HIV-1 diagnosed patients, ARV-naïve and followed-up in the University Hospital of Donka in Conakry, Guinea-Conakry, were included.
- ✓ Protease and reverse transcriptase genes were sequenced using the ANRS procedures.
- ✓ Drug resistance mutations were identified according to the 2009 update surveillance drug resistance mutations list (Bennett et al., PLoS One, 2009)
 - ✓ NRTI: 67E/G/N, 69D, 70E/R, 74I/V, 75A/M/S/T, 77L, 115F, 116Y, 151M, 184I/V, 210W, 215Y/F/I/S/C/D/V/E, 219E/N/Q/R
 - ✓ NNRTI: 100I, 101E/P, 103N/S, 106A/M, 179F, 181C/I/V, 188C/H/L, 190A/E/S, 225H, 230L
 - ✓ PI: 23I, 24I, 30N, 32I, 46I/L, 47A/V, 48M/V, 50L/V, 53L/Y, 54A/L/M/S/T/V, 73S, 73A/C/T, 76V, 82A/C/F/L/M/S/T, 83D, 84A/C/V, 85V, 88D/S, 90M
- ✓ Phylogenetic analyses were performed by estimating the relationships among RT sequences and reference sequences of HIV-1 genetic subtypes and circulating recombinant forms obtained from the Los Alamos Database (<http://hiv-web.lanl.gov>). Nucleotide sequences were aligned with the CLUSTAL W program version 1.7.29. Phylogenetic reconstruction was performed using a Kimura 2-parameter model and the neighbor-joining method.
- ✓ HIV tropism was assessed by gp120 sequencing, and interpreted with the Geno2Pheno (false positive rate: 10%) and PSSM algorithms.
- ✓ Plasma HIV-1 viral load was determined using the COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Test, v2.0 commercial assay. CD4 cell count was measured by flow cytometry using FACSCalibur (Becton Dickinson, San Jose, California, USA).
- ✓ Plasma concentrations of all ARV drugs were determined by HPLC coupled with fluorimetric detection.

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RESULTS

PATIENTS CHARACTERISTICS

Age [IQR] years (n=100)	39 [28-46]
Men (n=100)	30
Median CD4 (cells/mm ³) [IQR] (n=76)	223 [107-348]
Median HIV-1 plasma RNA (copies/mL) [IQR] (n=99)	88900 [20500-316400]
HIV-1 subtypes n	94
CRF02_AG	84
CRF09_cpx	4
A	3
D	1
G	1
F/BF	1
Viral Tropism n (%)	79
R5 Virus	63 (80%)
X4 Virus	5 (6%)
R5/X4 Virus *	11 (14%)

*Geno2Pheno and PSSM combined results

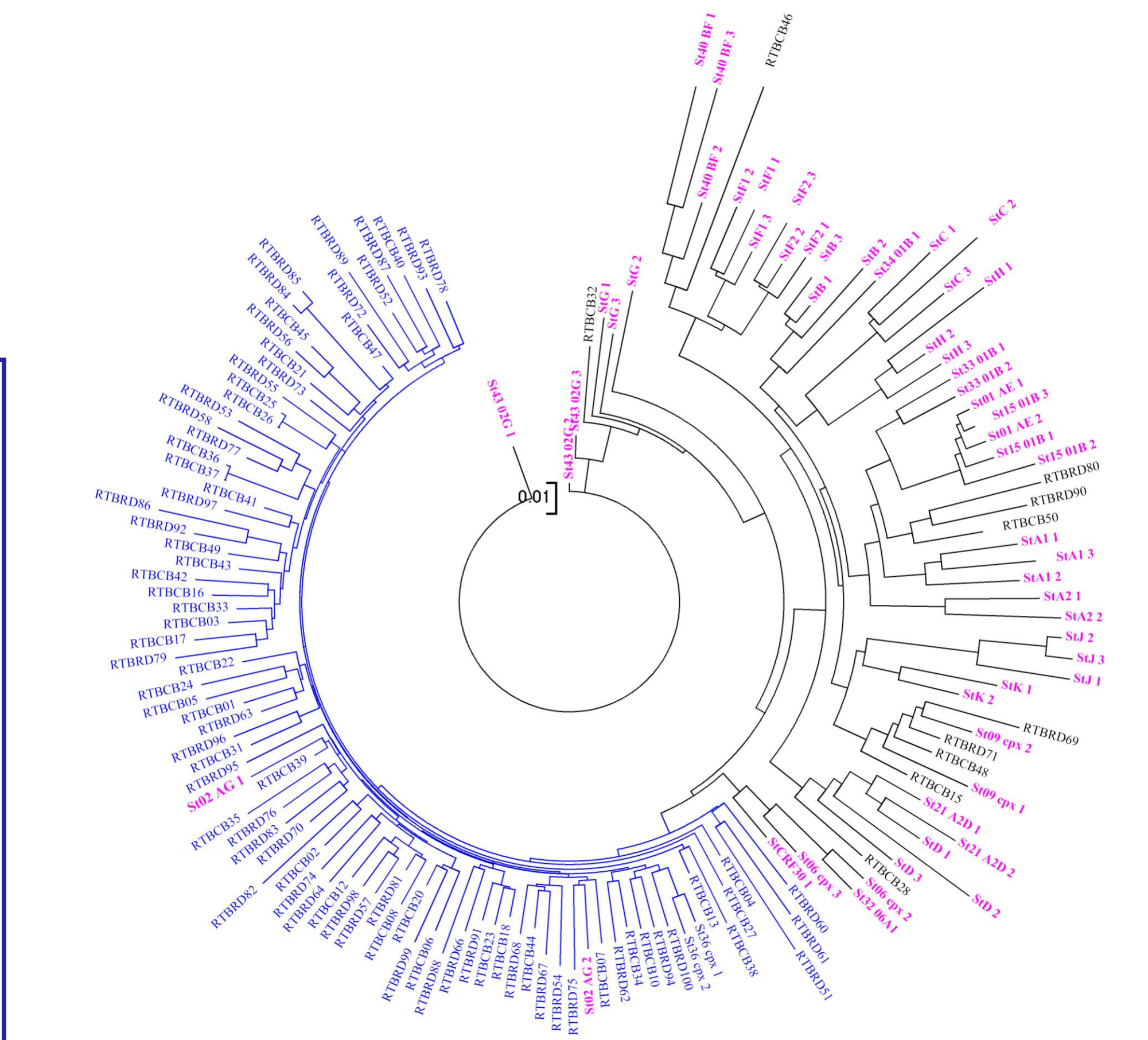
Resistance Associated Mutations

PATIENTS	HIV-1 SUBTYPE	NRTI	NNRTI	PI
3	CRF02_AG			I84V
5	CRF02_AG		K103N/S	
27	CRF02_AG	M184V	K103N, Y181C	
46	CRF02_AG	M41L, D67N, T69D, K70R, L74V, V75T, T215F, K219Q	Y181C, G190A	
48	CRF09_cpx		K103N, Y181C	
55	CRF02_AG	M184V	Y181C	
84	CRF02_AG		K101E	
85	CRF02_AG		K101E	
86	CRF02_AG		K103N	

Prevalence of virus with at least one mutation to NRTI, NNRTI and PI

	Total	NRTI	NNRTI	PI
Patients n=94	9	3	8	1
%	9.6	3.2	8.5	1
CI95	3.63 – 15.5	0.0 – 6.7	2.9 -14	0.0 – 3.1

- ✓ Protease and reverse transcriptase sequencing was successful in 94 (94%) samples.
- ✓ Most of the patients, 84 (89%), were infected with CRF02_AG recombinant virus.
- ✓ HIV tropism could be assessed in 79 samples, among them 63 (80%) were R5 viruses, 11 were R5X4 (14%), and 5 were X4 viruses (6%).
- ✓ Resistance analysis among the 94 samples showed that at least one drug resistance mutation was observed in 9 samples, leading to a prevalence of primary resistance of 9.6% [CI95], 3.63%-15.51%).
- ✓ NRTI resistance mutations were found in 3 samples (3.2%; CI95, 0.0%-6.7%). Among them, the M184V mutation was present in 2 cases. The remaining patient exhibited multiresistant virus harboring 8 NRTI mutations (M41L-D67N-T69D-K70R-L74V-V75T-T215F-K219Q).
- ✓ NNRTI mutations were detected in 8 samples (8.5%; CI95, 2.91%-14.11%). The most prevalent NNRTI mutations were the Y181C and K103N mutation, each detected in 4 cases. The K101E, K103S, and G190A mutations were detected in 2, 1, and 1 cases, respectively. 3 of NNRTI-resistant viruses exhibited 2 NNRTI-resistance mutations.
- ✓ Major PI mutation (I84V) was observed in one case (1%; CI95, 0.00%-3.06%).
- ✓ Overall, 3 patients of our series exhibited dual class-resistant viruses (3%; CI95, 0.00%-6.74%).
- ✓ ARV drug concentration measurements were performed in samples harboring drug resistance mutations (n = 9) and also in samples failing to be amplified for sequencing (n = 6), showing undetectable ARV plasma concentrations in all cases.



Phylogenetic relationships among Guinean HIV-1 group M RT sequences (n=94). Sequences issued from patients' virus are identified using numbers. Reference strains are included in the construction of the phylogenetic tree. Reference strains are in pink, CRF02_AG strains are in blue, others subtypes are in black.

CONCLUSIONS

A high prevalence of 9.6% of transmitted drug resistance was observed on this population of 100 ARV-naïve patients from Conakry, mostly infected with CRF02_AG viruses. Further surveillance in Conakry and in other cities of the country is warranted to precise the level and evolution of HIV-1 transmitted drug resistance in Guinea-Conakry.