Solthis
SOLIDARITÉ THÉRAPEUTIQUE & INITIATIVES CONTRE LE SIDA

Solidarité Thérapeutique et Initiatives contre le Sida

Résistance primaire en Guinée Conakry en 2009

Pr Diane Descamps
Virologie - GH Bichat-Claude Bernard
EA 4409

ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

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- Etude collaborative entre:
  - Laboratoire de Biologie du CHU de DONKA, Conakry – Pr Mandiou Diakite
  - Laboratoire de Virologie GH Bichat-Claude Bernard, Paris, Dr C Charpentier et Pr D Descamps
  - Laboratoire de Virologie, CHU de Bordeaux, Dr P Bellecave et Dr B Masquelier
  - ONG Solthis

- Depuis 2008, le laboratoire de Biologie du CHU de Donka réalise les charges virale VIH (Abbott)
- Conservé 100 plasma de patients naïfs d'ARV en 2009
- Tests de résistance génotypiques afin de déterminer la prévalence de la résistance primaire, les sous-types viraux et le tropisme

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

M Diakite, C Charpentier, P Bellecave, M Cisse, G Peytavin, B Djoudalbaye, L Pizzarro, C Katlama, F Huber, B Masquelier, D Descamps

Objective

- **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

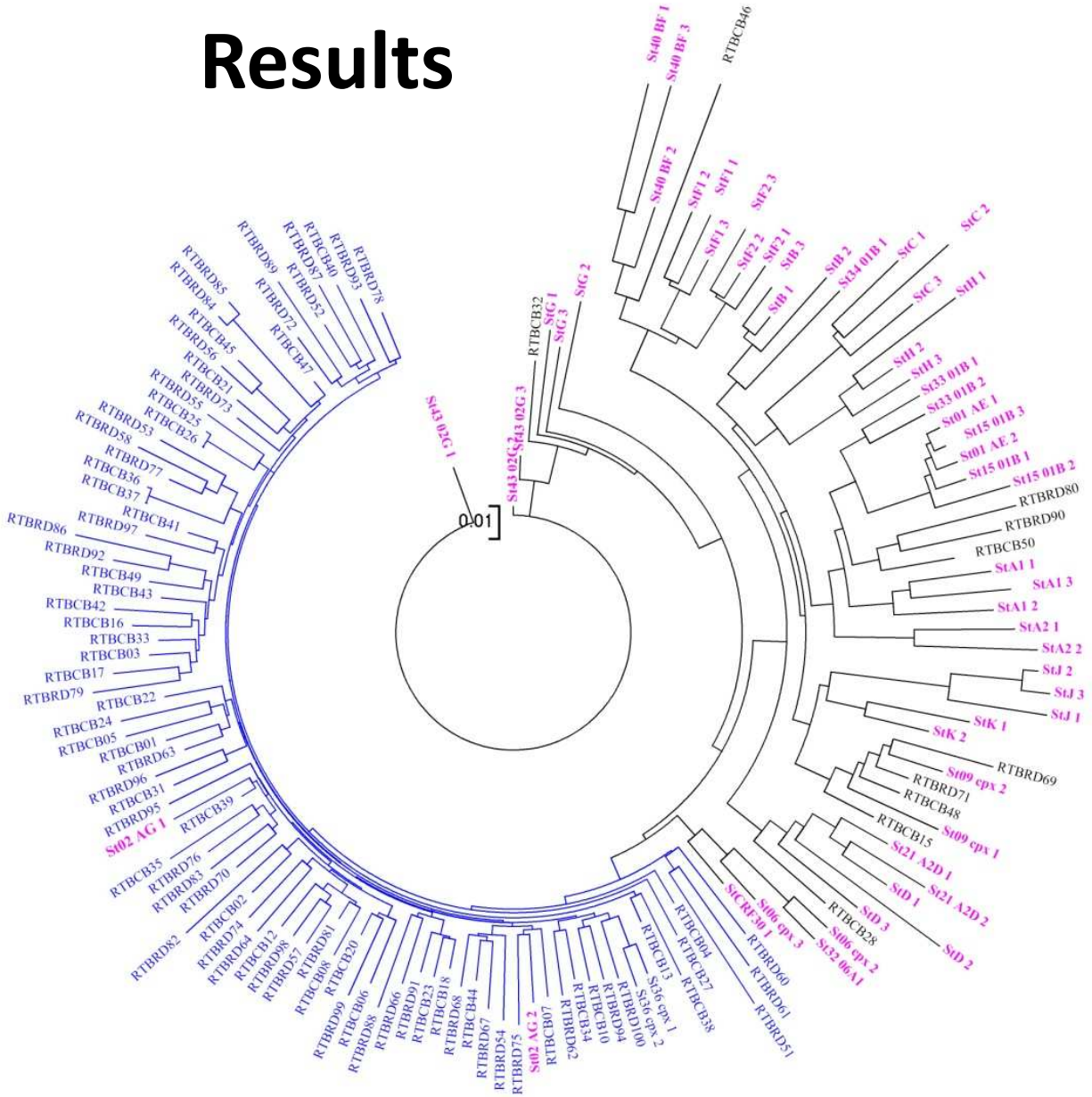
- ✓ **100 newly HIV-1 diagnosed patients, ARV-naïve and followed-up in the University Hospital of Donka in Conakry, Guinea-Conakry, were included.**
- ✓ **Protease and reverse transcriptase genes were sequenced using the ANRS procedures.**
- ✓ **Drug resistance mutations were identified according to the 2009 update surveillance drug resistance mutations list (Bennett et al., PLoS One, 2009)**
- ✓ **Phylogenetic analyses were performed using a Kimura 2-parameter model and the neighbor-joining method with 500 bootstrapped data sets.**
- ✓ **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.**
- ✓ **Plasma concentrations of all ARV drugs were determined by HPLC coupled with fluorimetric detection.**

Results

PATIENTS CHARACTERISTICS	
Age [IQR] years (n=100)	39 [28-46]
Men (n=100)	30
Median CD4 (cells/mm3) [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	

Results

Phylogenetic relationships among Guinean HIV-1 group M RT sequences (n =94). Sequeces issued from patients' virus are identified using numbers.
Refrence strains are in pink , CRF02_AG strains are in blue, others subtypes are in black.



Results

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

✓**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.**

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	

dual class-resistant viruses (3%; CI95, 0.00%-6.74%).

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.**
  - **Repeated studies on TDR including Donka CHU and La Carrière AIDS care Centers are planned in september on 200 patients**

International HIV Drug Resistance Workshop, Dubrovnik, Croatia, June 2010

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

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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: 67G/N, 69D, 70E/R, 74V/I, 75A/M/S/T, 77L, 115F, 116Y, 151M, 184I/V ,210W, 215Y/F,I/S,C/D/V/E,219Q/N/Q/R
  - NNRTI:100I,101E/P,103N/S,106A/M,179E,181C/I/V,188C/H/L,190A/E/S,225H, 230L
  - PI: 10I,20I,30N,32I, 46I/L, 47A/V,48M/V, 50L/V, 53L/Y, 54A/L/M/S/T/V, 73S/A/C/T, 74V, 82A/C/F/I/M/S/T, 84C, 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 1.7.2S. Phylogenetic reconstruction was performed using a Kimura 2-parameter model and the neighbor-joining method with 100 bootstrapped data sets.
- 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.

ACKNOWLEDGMENTS

We thank Adolphe Kolié Yarannou and Alpha Amadou Sank Diallo (Donka) and Juliette Leleu and Alexandre Storto (Paris) for helpful technical assistance.

RESULTS

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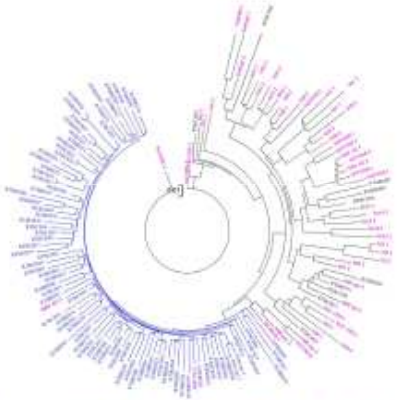
✓Protease and reverse transcriptase sequencing was successful in 94 (94%) patients.
✓Most of the patients, 84 (89%), were infected with CRF02_AG recombinant virus.
✓HIV tropism could be assessed in 79 samples, among them 63 (80%) were R5 viruses, 11 were R5X4 (14%), and 5 were X4 viruses (6%).
✓Resistance 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.



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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.

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Dr Stephanie Tchiombiano

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SEVENTH FRAMEWORK PROGRAMME

Collaborative HIV and Anti-HIV Drug Resistance Network

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