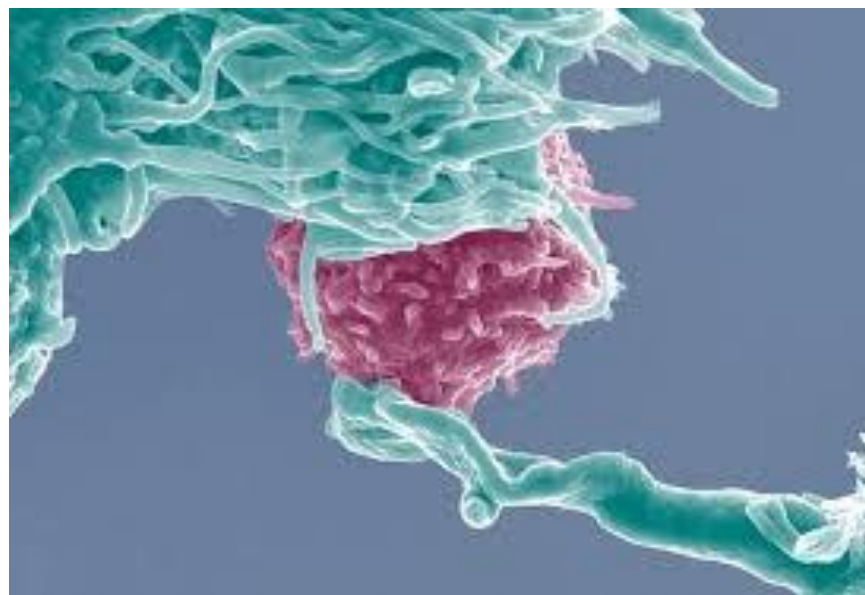


# Genetic Diversity of HIV-1 and Profile of Drug Resistance in Tunisia

**El Moussi Awatef, Salma Abid, Majda Nasr, Dorra Arab,  
Ichrak Landolsi, Latifa Charaa  
& Pr Amine Slim**

**National Centre of HIV, Microbiology Laboratory,  
Charles Nicolle University Hospital , Tunis, Tunisia**

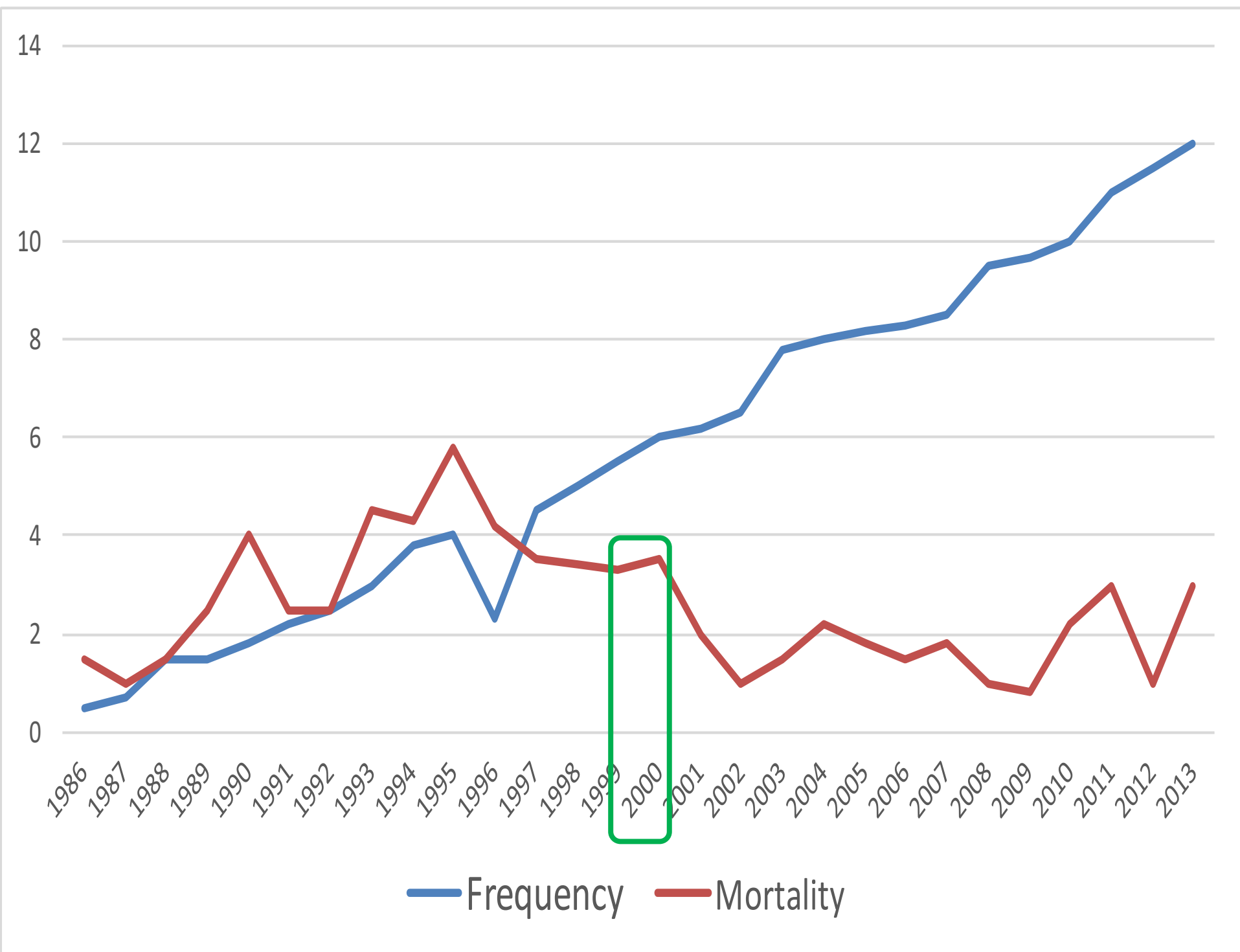


# Outline

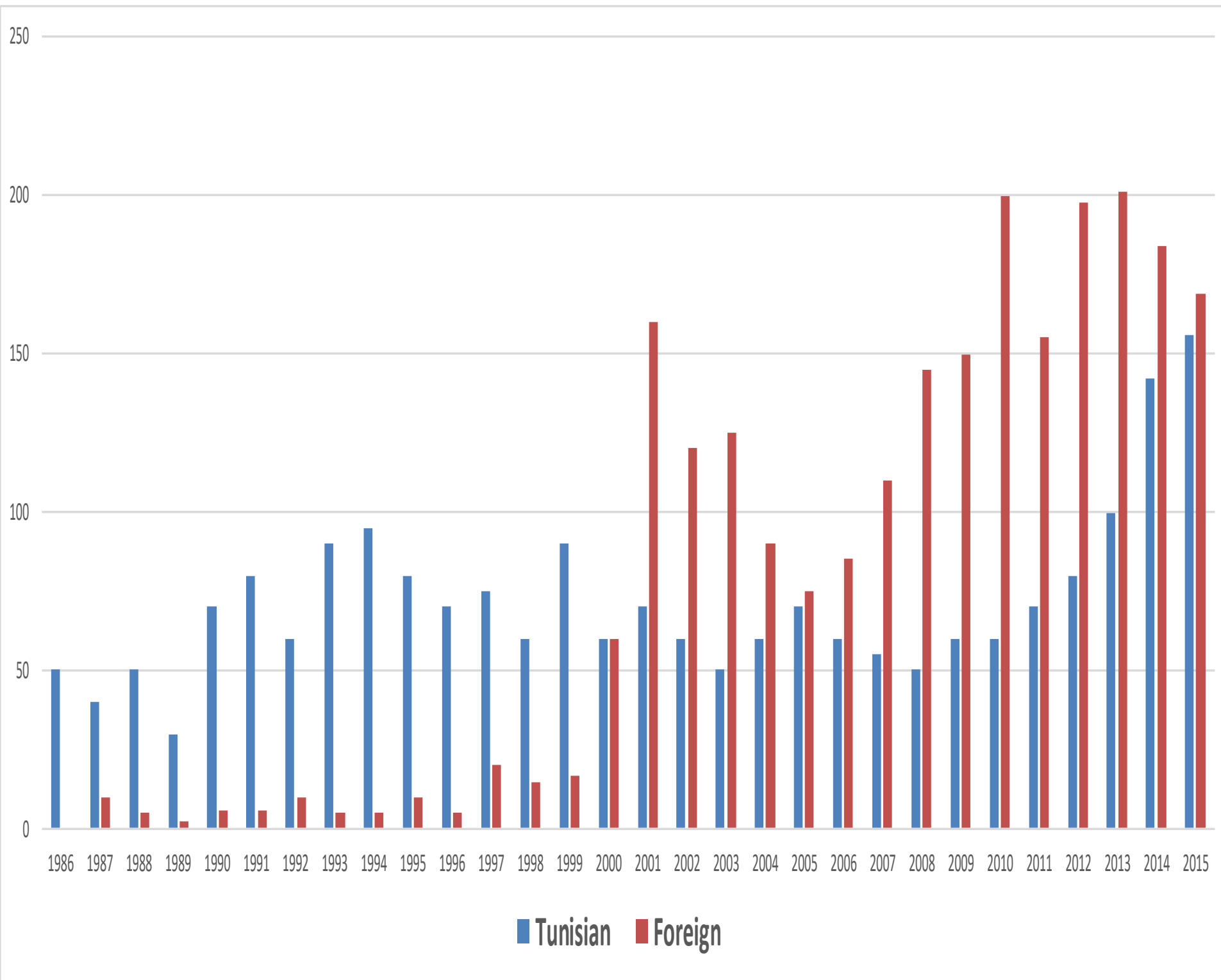
- I. Epidemiological situation of HIV-1 in Tunisia**
- II. Distribution of all HIV-1 sequences: WORLD**
- III. Genetic Distribution of HIV-1 in Tunisia**
- IV. Drug Resistance in Tunisia**
- V. Conclusion and perspectives**

# **Epidemiological situation of HIV-1 in Tunisia**

# Evolution of the prevalence and mortality (100,000 Inhabitants) of HIV / AIDS in Tunisia between 1986-2013

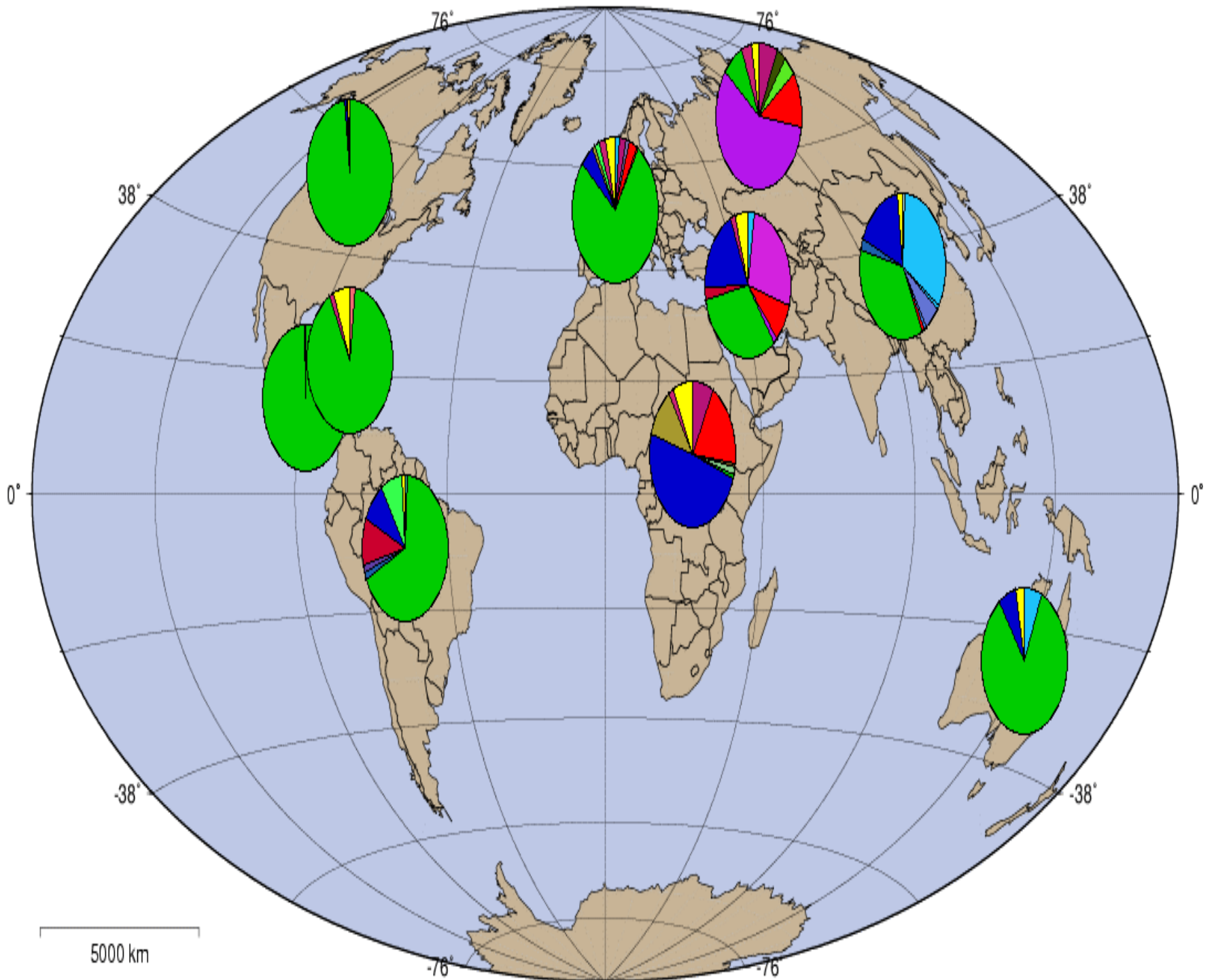


# Evolution of new cases of HIV / AIDS cases detected in Tunisia \_1986-2015

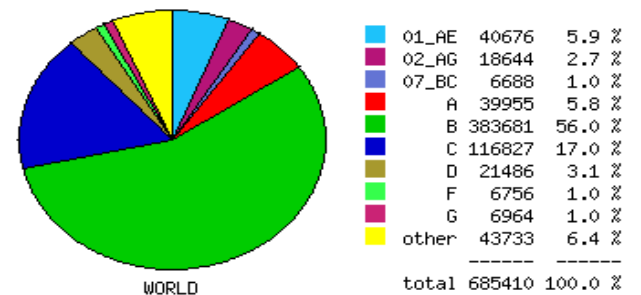


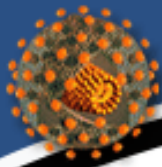
- Until **2015** a total of **2159** cases of HIV-1 infection were registered.
- of which **612** correspond to persons who have died.
- The HIV prevalence in Tunisia is **14.4/100,000** inhabitants, which has remained relatively stable over recent years, placing Tunisia among the low prevalence countries.
- The main mode of transmission is through **heterosexual** contact (45.34%), followed by injection **drug** use (21.44%), **homosexual** contact (5.32 %), **mother to child** transmission (4.58%) and for 18.2% the transmission route is unknown.

# Distribution of all HIV-1 sequences: WORLD

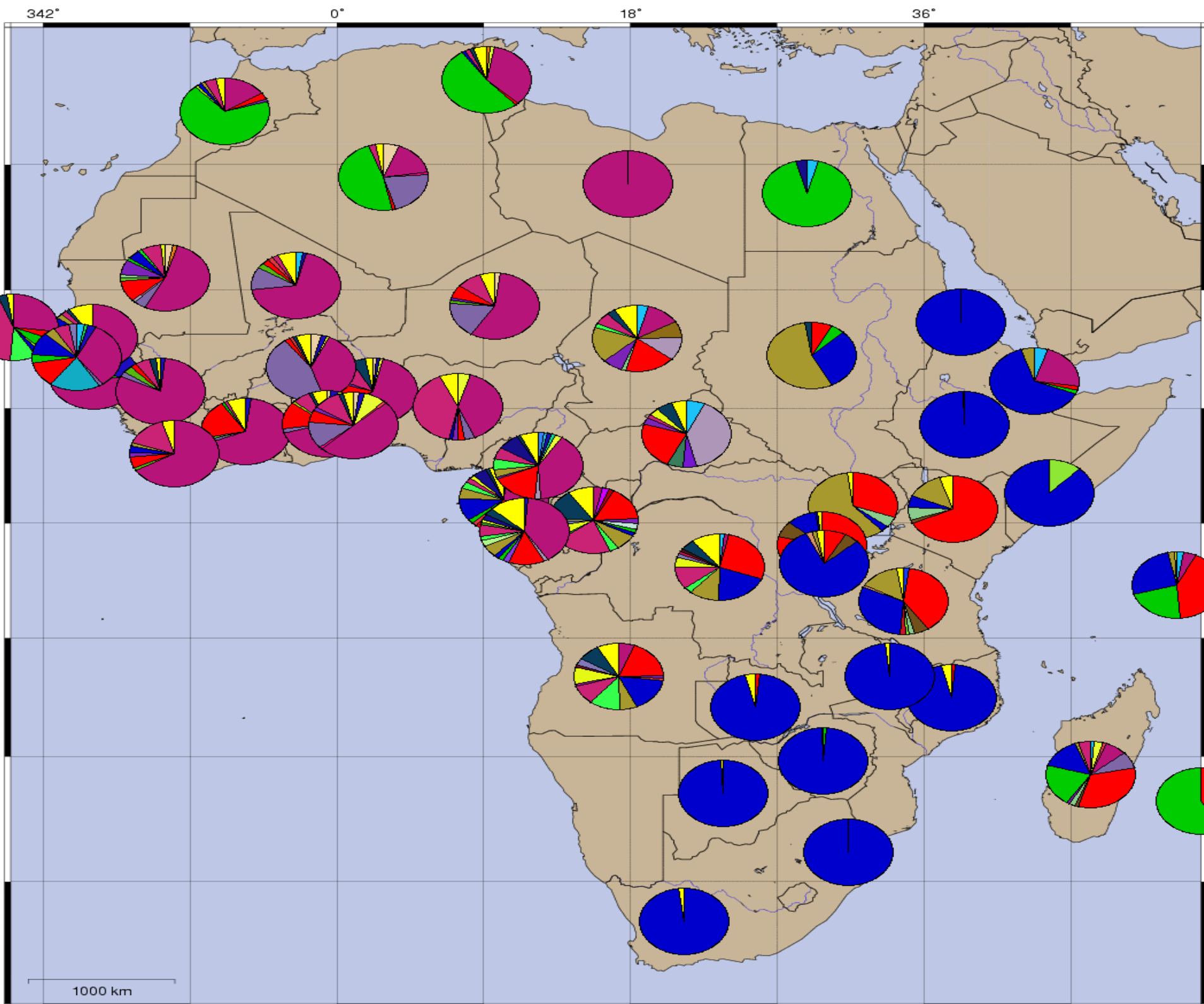


GMT 2003 Mar 11 09:23:31 IGMR 1.2





# HIV sequence database



GMT 2003 Apr 1 10:26:30 IGNIT 1.2



Clade	Count	Percentage
O2_AG	13521	7.8 %
A	33301	19.3 %
A1C	1491	0.9 %
A1D	2626	1.5 %
B	1646	1.0 %
C	84956	49.2 %
D	19268	11.2 %
G	2987	1.7 %
other	12977	7.5 %
-----		
total	172773	100.0 %

AFRICA



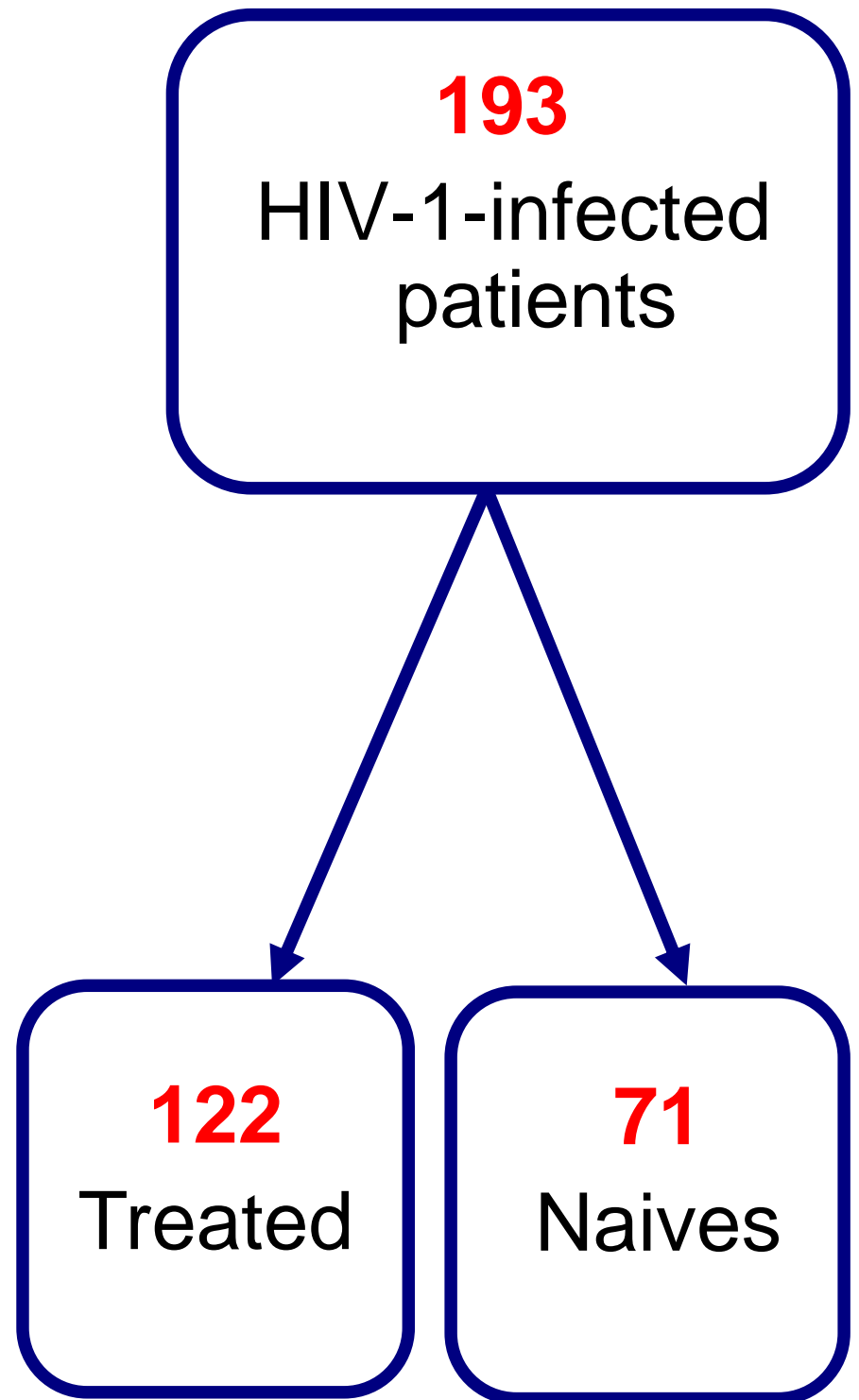
# **Genetic Distribution of HIV-1 in Tunisia!!**

- We investigate HIV-1 infection in Tunisia in samples collected during three years 2012-2015.
- The objective of updating the information on HIV-1 **genetic diversity** in the country and the prevalence of **resistance to anti-retroviral treatments**.

# Material

ID	Hopital	Date Preleveme	Stade
1	4548 Rabta Tunis	19/04/2014	Bilan Initial
2	6703 Pneumo CHU	09/06/2014	Bilan Initial
3	6656 Rabta Tunis	07/06/2014	Bilan Initial
4	6629 Rabta Tunis	07/06/2014	Bilan Initial
5	9584 Rabta Tunis	30/08/2014	Bilan Initial
6	6299 Rabta Tunis	31/05/2014	C3
7	6031 Rabta Tunis	24/05/2014	C3
8	5066 Rabta Tunis	03/05/2014	Bilan Initial
9	7101 Rabta Tunis	21/06/2014	C3
10	6881 Rabta Tunis	14/05/2014	Bilan Initial
11	7622 Rabta Tunis	05/07/2014	Bilan Initial
12	7619 Rabta Tunis	05/07/2014	Bilan Initial
13	7359 Rabta Tunis	28/06/2014	Bilan Initial
14	7629 Rabta Tunis	05/07/2014	Bilan Initial
15	7786 CHU Monastir	10/07/2014	
16	7905 Rabta Tunis	12/07/2014	Bilan Initial
17	8191 Rabta Tunis	19/07/2014	A3
18	7106 Rabta Tunis	21/06/2014	A1
19	8392 Rabta Tunis	26/07/2014	Bilan Initial
20	5762 Rabta Tunis	17/05/2014	Bilan Initial
21	6945 Labo privé Nao	17/06/2014	Bilan Initial
22	7254 Labo privé Barc	25/06/2014	Bilan Initial
23	21 Clinique Taoufi	02/01/2014	Bilan Initial
24	796 Dispensaire 9 / 23	01/2014	Bilan Initial
25	1368 Labo privé Feni	06/02/2014	Bilan Initial
26	7628 Rabta Tunis	05/07/2014	B1
27	9029 Rabta Tunis	16/08/2014	Bilan Initial
28	7375 Rabta Tunis	28/06/2014	Bilan Initial
29	5415 Rabta Tunis	10/05/2014	Bilan Initial
30	7907 Rabta Tunis	12/07/2014	Bilan Initial
31	9872 Rabta Tunis	06/09/2014	C3 (Toxicocerebrale)
32	10393 Rabta Tunis	20/09/2014	B2
33	10403 Rabta Tunis	20/09/2014	C3
34	1181 Rabta Tunis	01/02/2014	B3
35	1272 CHU Monastir	03/02/2014	A3
36	1502 Rabta Tunis	08/02/2014	Centre Afrique
37	889 Rabta Tunis	25/01/2014	C3
38	10395 Rabta Tunis	20/09/2014	B
39	11643 Rabta Tunis	18/10/2014	C3
40	12296 Rabta Tunis	01/11/2014	Bilan Initial
41	12297 Rabta Tunis	01/11/2014	C3
42	12605 Rabta Tunis	08/11/2014	Bilan Initial
43	4100 Rabta Tunis	08/04/2014	Bilan Initial
44	4545 Rabta Tunis	19/04/2014	Bilan Initial
45	6638 Rabta Tunis	07/06/2014	C3
46	6307 Rabta Tunis	31/05/2014	C3
47	3921 Rabta Tunis	05/04/2014	Bilan Initial
48	6037 Rabta Tunis	24/05/2014	Bilan Initial
49	5419 Rabta Tunis	10/05/2014	C3
50	7370 Rabta Tunis	28/06/2014	Bilan Initial
51	6654 Rabta Tunis	07/05/2014	Bilan Initial
52	7365 Rabta Tunis	28/06/2014	C3
53	7624 Rabta Tunis	05/07/2014	Bilan Initial
54	7630 Rabta Tunis	05/07/2014	C3
55	7627 Rabta Tunis	05/07/2014	Bilan Initial

56	7908 Rabta Tunis	12/07/2014	C3
57	7360 Rabta Tunis	28/06/2014	A1
58	7898 Rabta Tunis	12/07/2014	Bilan Initial
59	6946 Labo privé Nao	17/06/2014	Bilan Initial
60	241 CHU Marsa	09/01/2014	Bilan Initial
61	8898 Rabta Tunis	09/08/2014	Bilan Initial
62	4637 Labo privé Fatn	22/04/2014	Bilan Initial
63	1701 CHU Farhat Ha	12/02/2014	
64	9310 Rabta Tunis	23/08/2014	Lybie
65	10108 Rabta Tunis	13/09/2014	C3
66	10396 Rabta Tunis	20/09/2014	C3
67	10767 Rabta Tunis	27/09/2014	Bilan Initial
68	1186 Rabta Tunis	01/02/2014	C3
69	1491 Rabta Tunis	07/02/2014	C3
70	1660 CHU Hedi Chal	12/02/2014	
71	9869 Rabta Tunis	06/09/2014	B3
72	11642 Rabta Tunis	18/10/2014	
73	11745 CHU Monastir	21/10/2014	B
74	12494 CHU Hedi Chal	06/11/2014	B
75	12610 Rabta Tunis	08/11/2014	B
76	13313 Rabta Tunis	24/11/2014	femme enceinte
77	13309 Rabta Tunis	25/11/2014	B3
78	11141 CHU Farhat Ha	08/10/2014	
79	11246 CHU Farhat Ha	10/10/2014	
80	12946 Rabta Tunis	15/11/2014	C
81	12956 Rabta Tunis	15/11/2014	C3
82	11630 Rabta Tunis	18/10/2014	
83	12295 Rabta Tunis	01/11/2014	Bilan Initial
84	12954 Rabta Tunis	15/11/2014	
85	14242 Rabta Tunis	13/12/2014	
86	14559 Rabta Tunis	20/12/2014	A1
87	14566 Rabta Tunis	20/12/2014	B femme enceinte
88	14569 Rabta Tunis	20/12/2014	Bilan Initial
89	14889 Rabta Tunis	27/12/2014	Bilan Initial
90	13941 Rabta Tunis	16/12/2014	C3
91	14890 Rabta Tunis	27/12/2014	C3
92	153 Rabta Tunis	07/01/2015	C3
93	423 Rabta Tunis	12/01/2015	C3
94	408 Rabta Tunis	10/01/2015	C3
95	402 Rabta Tunis	10/01/2015	C3
96	748 Rabta Tunis	17/01/2015	C3
97	754 Rabta Tunis	17/01/2015	C3
98	403 Rabta Tunis	10/01/2015	B
99	1544 Rabta Tunis	31/01/2015	C3
100	1548 Rabta Tunis	31/01/2015	B (Guiné)
101	1538 Rabta Tunis	01/01/2015	
102	1531 Rabta Tunis	31/01/2015	
103	1532 Rabta Tunis	31/01/2015	Bilan Initial
104	1529 Rabta Tunis	31/01/2015	B
105	409 Rabta Tunis	10/01/2015	C3
106	1890 Rabta Tunis	07/02/2015	
107	1677 CHU Farhat Ha	04/02/2015	
108	1662 CHU Monastir	04/02/2015	C3
109	3393 Rabta Tunis	07/03/2015	Bilan Initial
110	1541 Rabta Tunis	31/01/2015	C3
111	2809 Hopital Ariana	25/02/2015	Bilan Initial
112	3651 Hopital Militaire	12/03/2015	Bilan Initial
113	3843 Rabta Tunis	14/03/2015	Bilan Initial
114	3842 Rabta Tunis	14/03/2015	A2

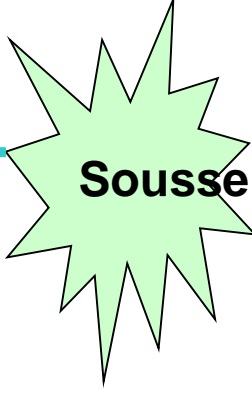




Infectious Diseases Department, Rabta University Hospital.



Infectious Diseases Department, Farhat Hached University Hospital.



Infectious Diseases Department, Fatouma Bourguiba University Hospital.



Infectious Diseases Department, Hedi Chaker University Hospital.





# Sequence Analysis procedures

## Sequence processing

Assemble:



*SeqMan* SeqScape

Edit & Align:



*BioEdit*

*ClustalX*



Version 7.0  
2014 Feb 27



Analysis

ARV resistance mutations:



Intersubtype recombination:



*RIP*  
*Online: REGA*  
*Genotyping*



Quality Control

Local BLAST:  *BioEdit*

Phylogenetic tree: *MEGA*

Links:



# Algorithm of Stanford University

## HIVdb: Genotypic Resistance Interpretation Algorithm

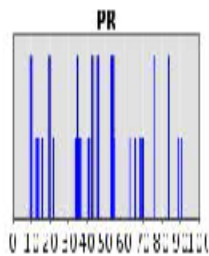
Date: 23-Feb-2015 18:17:19 UTC Filename: TN1890\_PRT\_ARNS.fas

Seq ID: 15TN1890\_PRT

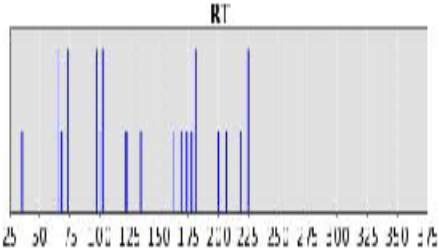
2. RT: CRF02\_AG (92.4%)

### Sequence Quality Assessment

Gene	QA Problem	Codons
PR	Stop Codons, Frame Shifts:	None
PR	Ambiguous Positions:	None
PR	Unusual Residues:	None



Gene	QA Problem	Codons
RT	Stop Codons, Frame Shifts:	None
RT	Ambiguous Positions:	None
RT	Unusual Residues:	None



Blue lines indicate differences from consensus B; tall blue lines indicate sites associated with drug resistance. Red lines indicate QA problems.

### Drug Resistance Interpretation: PR

PI Major Resistance Mutations: M46I, I54V, L76V, I84V

PI Minor Resistance Mutations: L10V, K20I, E35G, K43T, F53L

Other Mutations: I13A, K14R, G18E, A22V, E34D, M38I, N37D, R41K, K55R, L83R, I88F, H89K, K70R, L89I, T91S

#### Protease Inhibitors

atazanavir (ATV/r)	High-level resistance
darunavir (DRV/r)	Intermediate resistance
fosamprenavir (FPV/r)	High-level resistance
indinavir (IDV/r)	High-level resistance
lopinavir (LPV/r)	High-level resistance
nelfinavir (NFV)	High-level resistance
saquinavir (SQV/r)	High-level resistance

### PR Comments

#### PIMajor

- ◆ M46I/L are nonpolymorphic PI-selected mutations that reduce susceptibility to IDV, NFV, FPV, LPV and ATV when present with other mutations. M46L also reduces susceptibility to TPV.
- ◆ I54V is a nonpolymorphic mutation selected primarily by IDV and LPV. It reduces susceptibility to each of the PIs except DRV. It synergistically reduces PI susceptibility when present in combination with V82 mutations.
- ◆ L76V is a nonpolymorphic mutation selected by IDV, LPV and DRV. It reduces susceptibility to these PIs and to FPV. It increases susceptibility to ATV, SQV and TPV. L76V is included in the Tibotec DRV GSS.
- ◆ I84V is a nonpolymorphic substrate-cleft mutation selected by each of the PIs. It causes high-level resistance to ATV, FPV, IDV, NFV and SQV, intermediate-level resistance to LPV and TPV, and low-level resistance to DRV.

#### PIMinor

- ◆ L10I/V are polymorphic, PI-selected accessory mutations that reduce PI susceptibility or increase the replication of viruses with other PI-resistance mutations.
- ◆ K20I is the consensus amino acid in subtype G and CRF02\_AG. In subtypes B and C, K20I is a PI-selected mutation that appears to reduce NFV susceptibility.
- ◆ E35G is a relatively nonpolymorphic PI-selected mutation that is weakly associated with reduced NFV and TPV susceptibility.
- ◆ K43T is a nonpolymorphic PI-selected accessory mutation that, in combination with other PI-resistance mutations, is associated with reduced susceptibility to most PIs. It is also part of the GSS for TPV.
- ◆ F53L is a nonpolymorphic mutation selected primarily by SQV, IDV, ATV, and LPV. It reduces susceptibility primarily to ATV, SQV, and NFV. F53Y is a rare nonpolymorphic PI-selected mutation that has not been well studied.

#### Other

- ◆ L88T/I are nonpolymorphic PI-selected mutation of uncertain phenotypic and clinical significance.

### Drug Resistance Interpretation: RT

NRTI Resistance Mutations: K65R, L74I

NNRTI Resistance Mutations: A98G, K103N, Y181C, P225H

Other Mutations: V35A, S88G, T89I, K101R, K122E, D123N, I135L, S182A, E188K, K173A, Q174N, D177E, I178M, T200A, Q207E, K219H

#### Nucleoside RTI

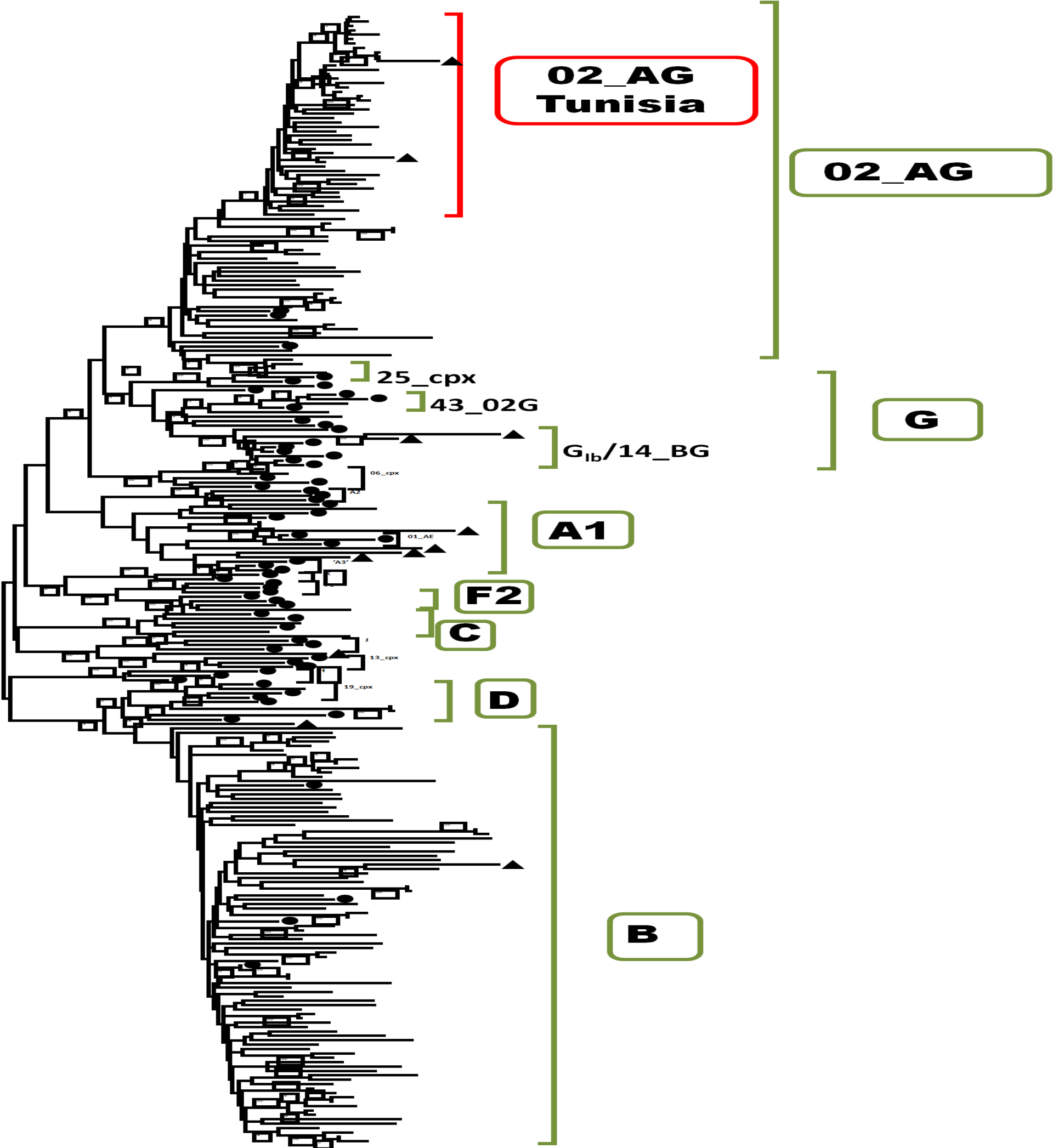
lamivudine (3TC)	Intermediate resistance
abacavir (ABC)	High-level resistance
zidovudine (AZT)	Susceptible
stavudine (D4T)	Intermediate resistance
didanosine (DDI)	High-level resistance
emtricitabine (FTC)	Intermediate resistance
tenofovir (TDF)	High-level resistance

#### Non-Nucleoside RTI

efavirenz (EFV)	High-level resistance
etravirine (ETR)	Intermediate resistance
nevirapine (NVP)	High-level resistance
rilpivirine (RPV)	Intermediate resistance

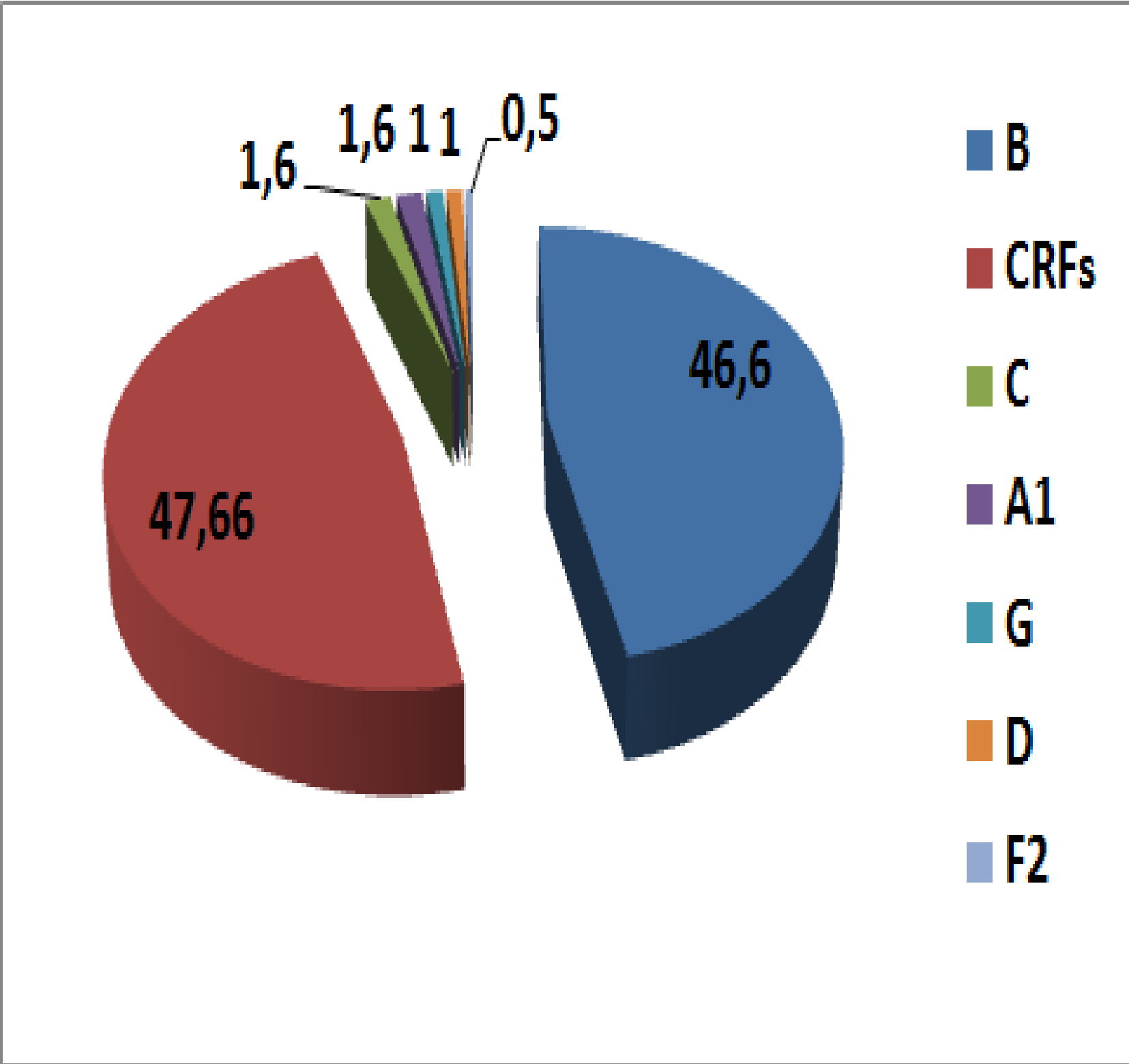
# Phylogenetic analysis of HIV-1 in Tunisia



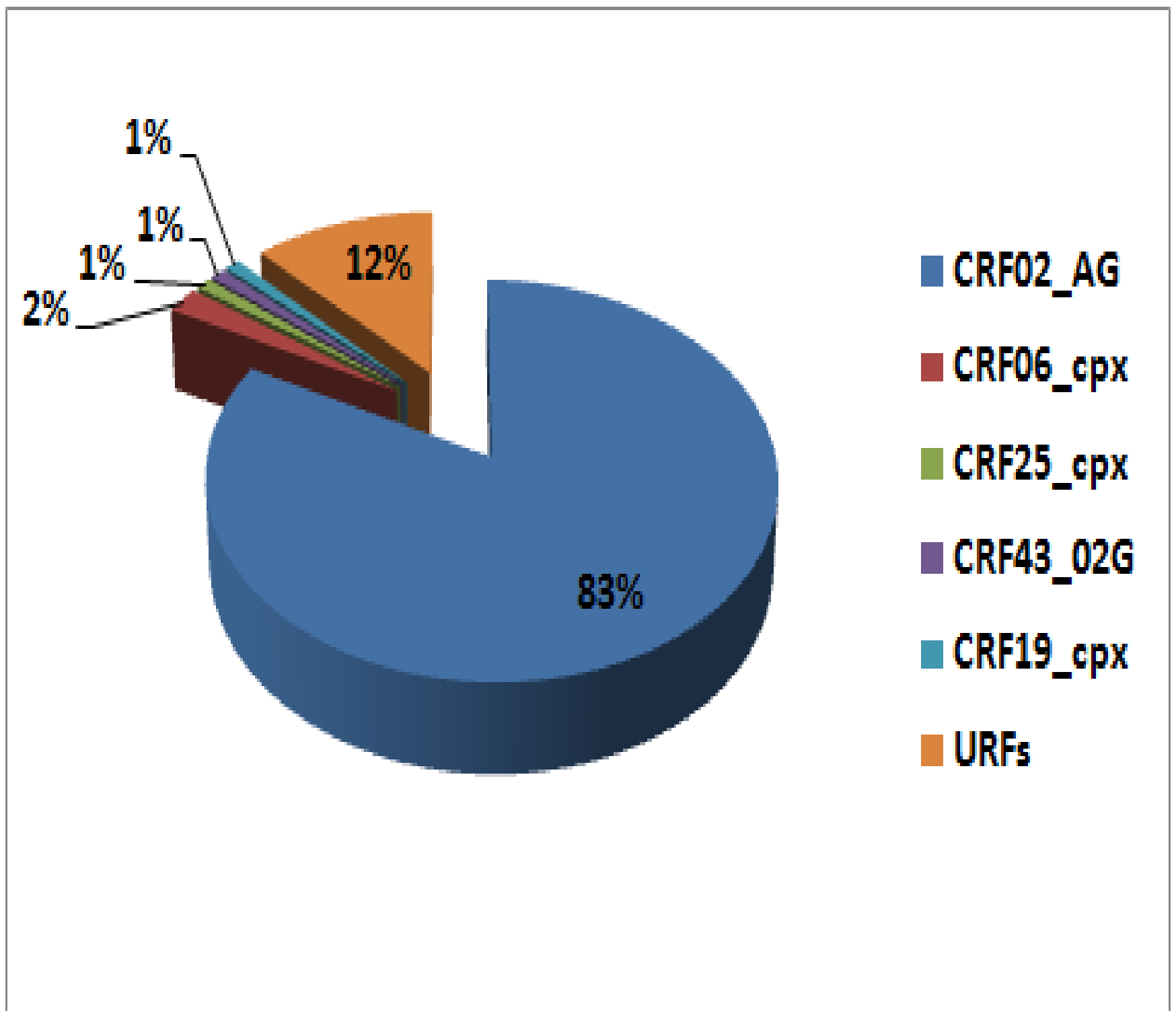


Maximum likelihood phylogenetic tree of 193 HIV-1 PR-RT sequences from Tunisia

# Distribution of genetic forms of VIH-1 in Tunisia



# Distribution of CRFs in Tunisia



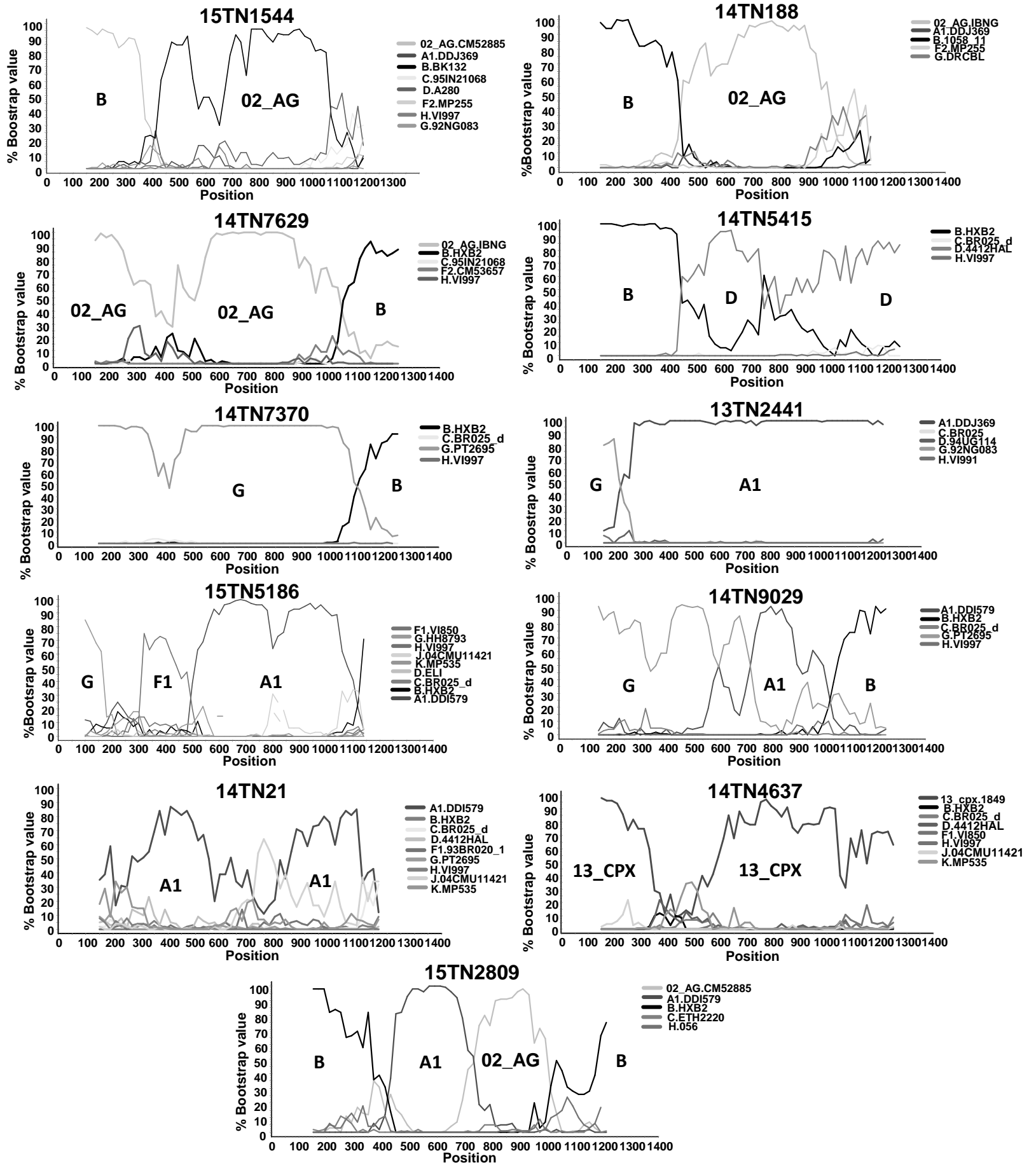
**CRF02\_AG-----A and G**

**CRF06\_cpx-----A, G, J and K**

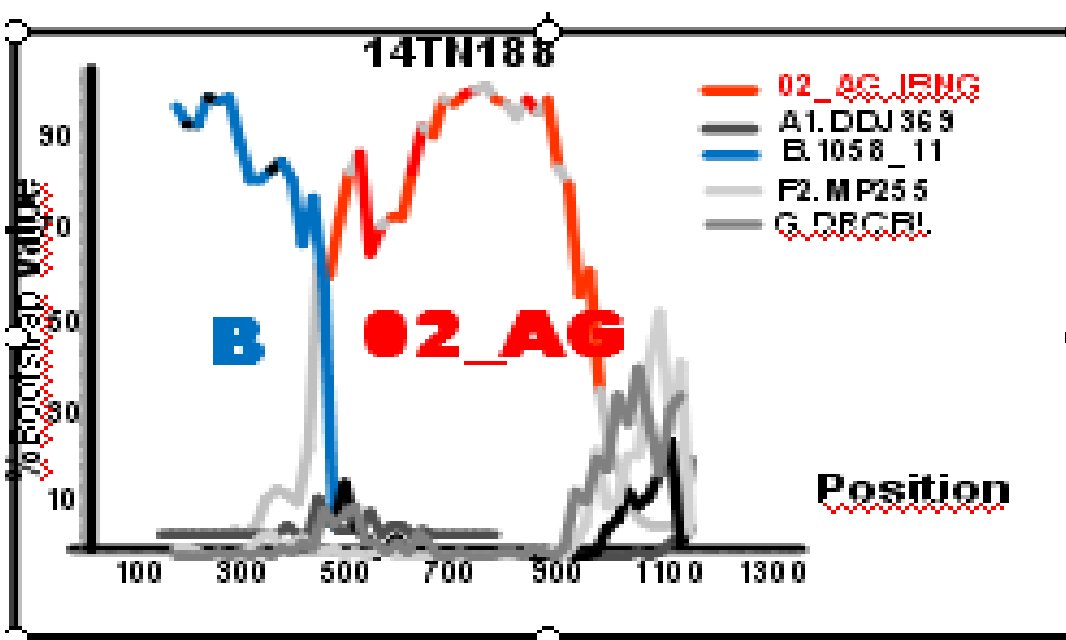
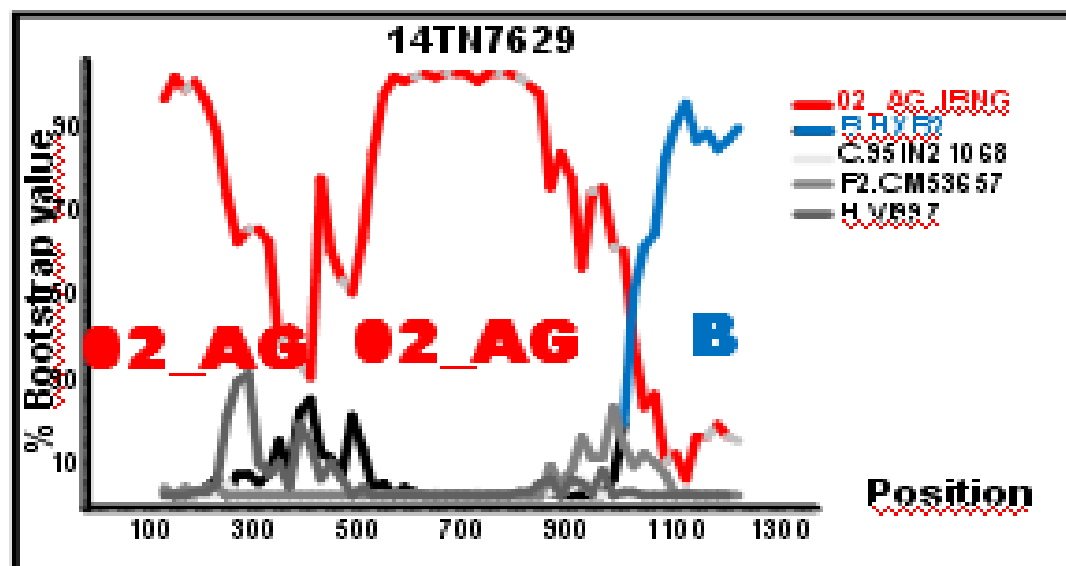
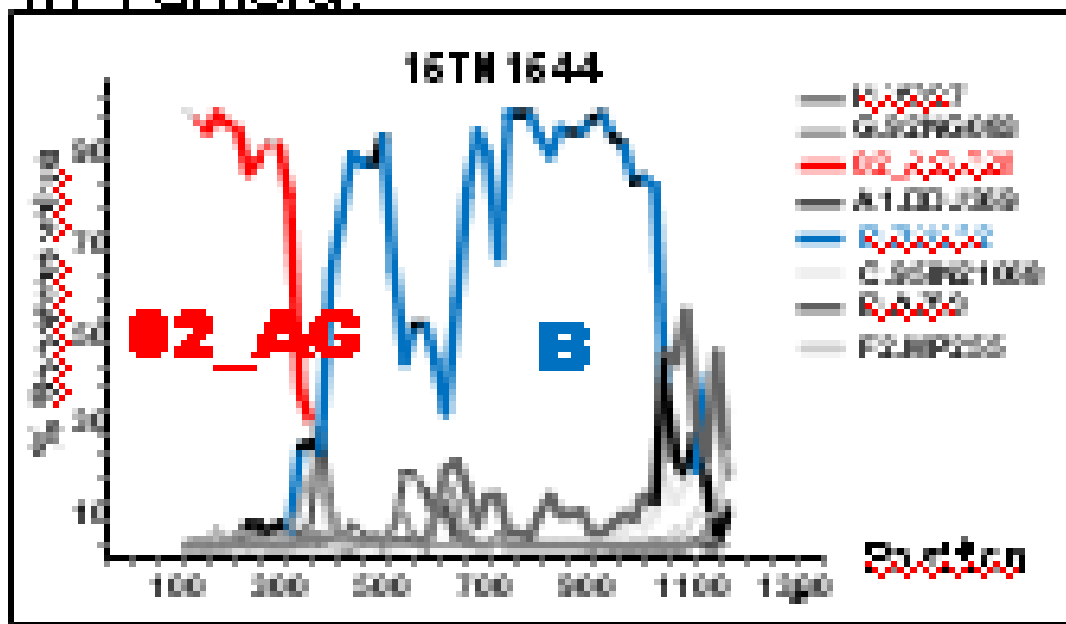
**CRF25\_cpx-----A, G and U**

**CRF43\_02AG---CRF02\_AG and G**

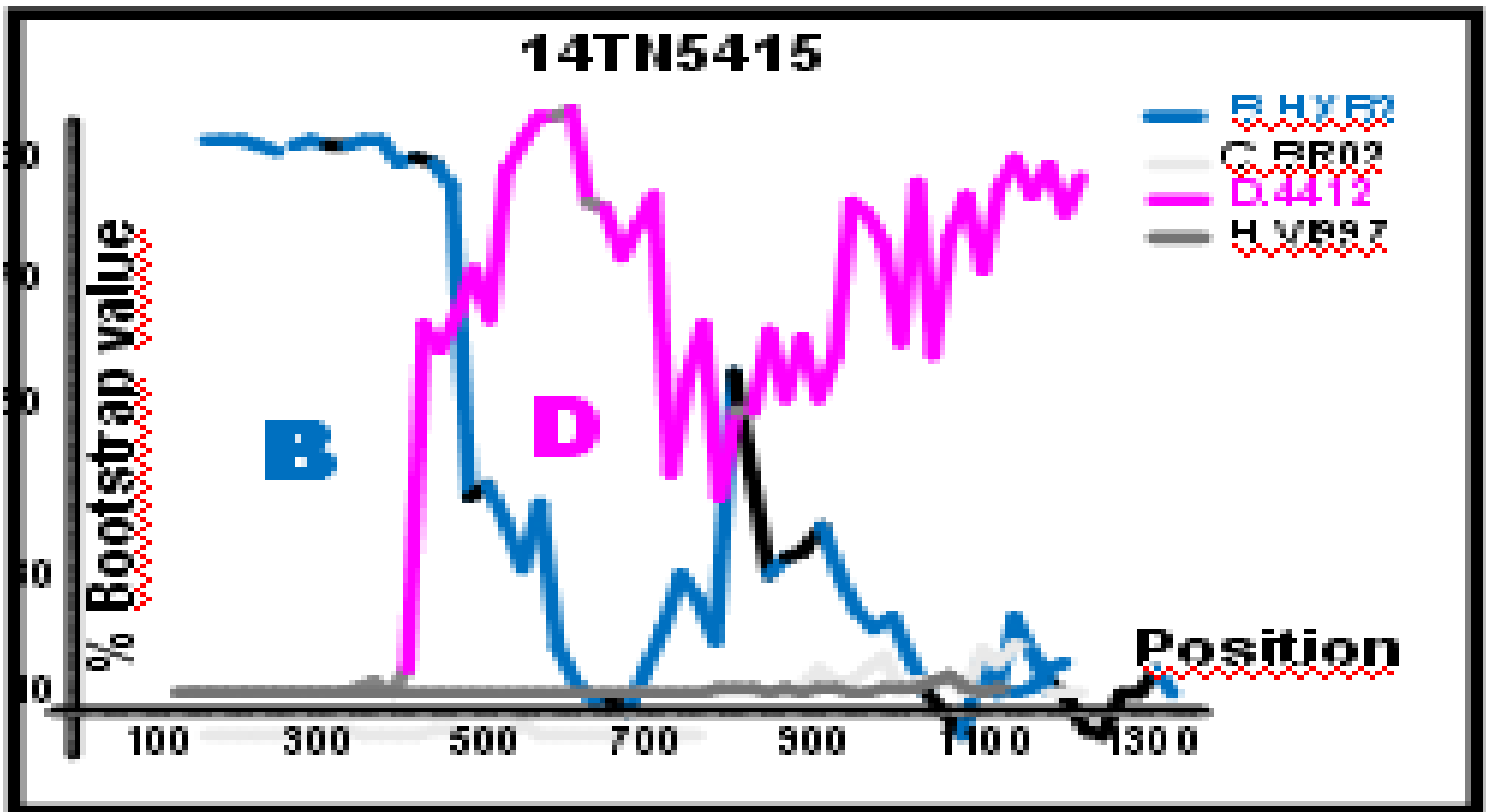
**CRF19\_cpx---A1, D and G**



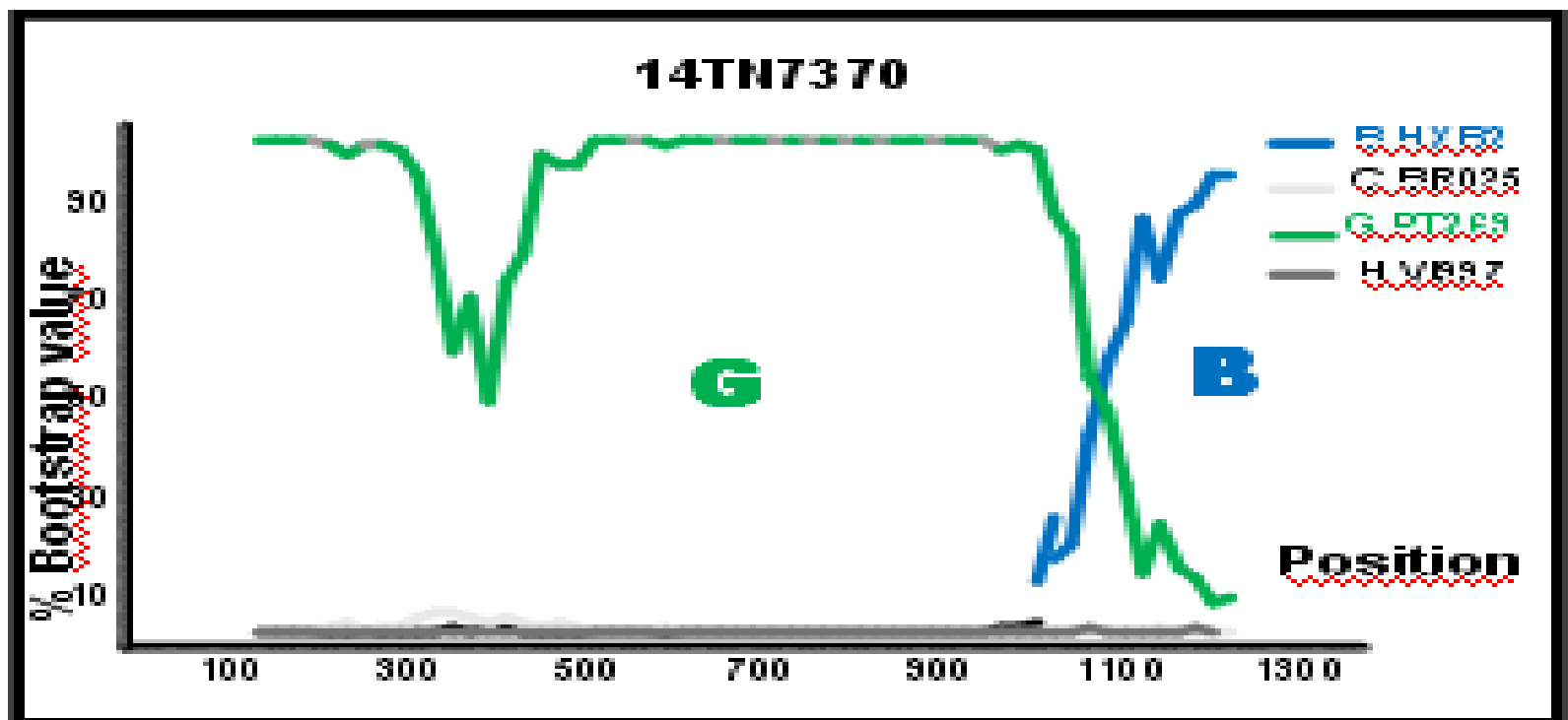
**Bootscan plots of PR-RT sequences of 11 HIV-1 URFs identified in Tunisia**



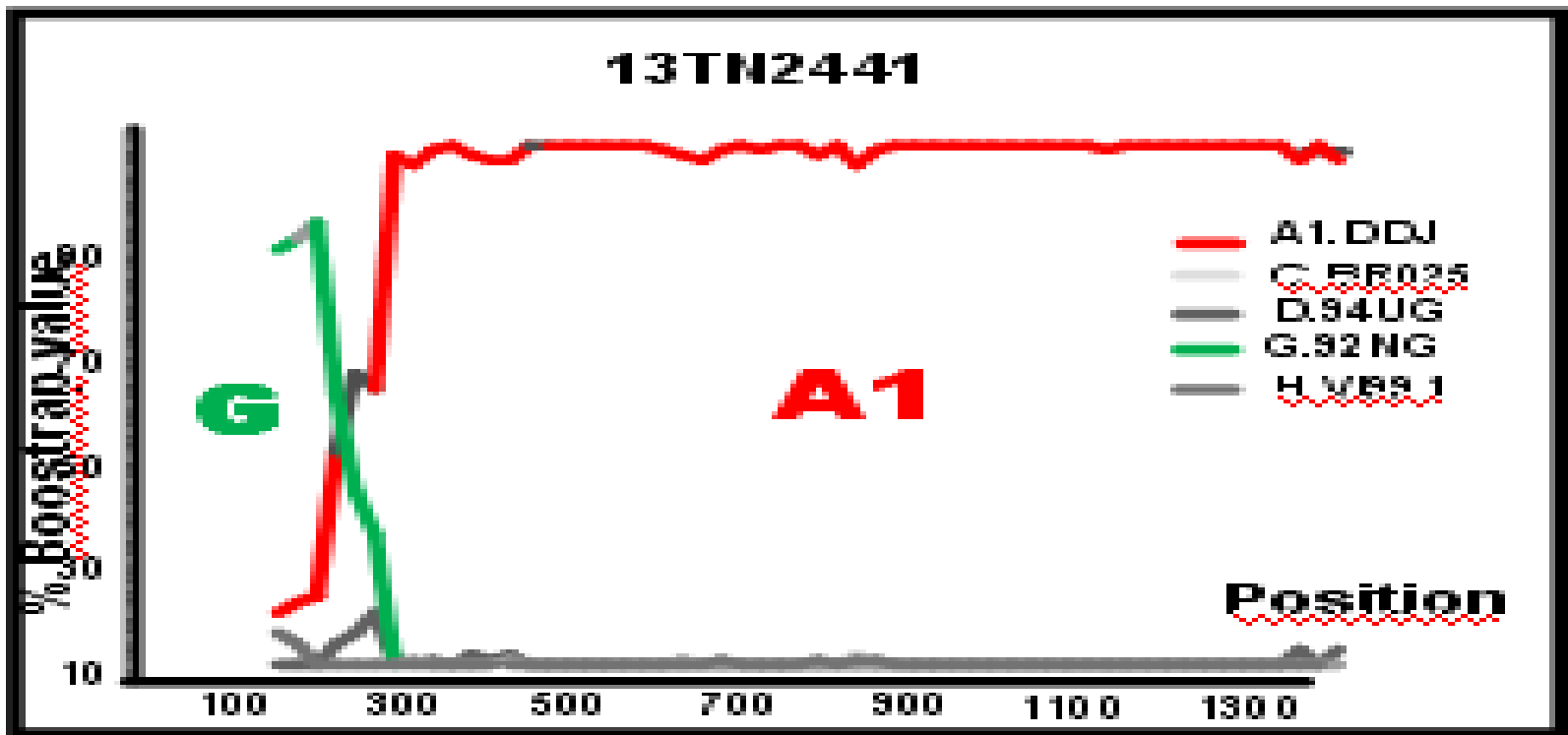
3 Tunisian URFs **B/ CRF02\_AG** with different positions of breakpoints



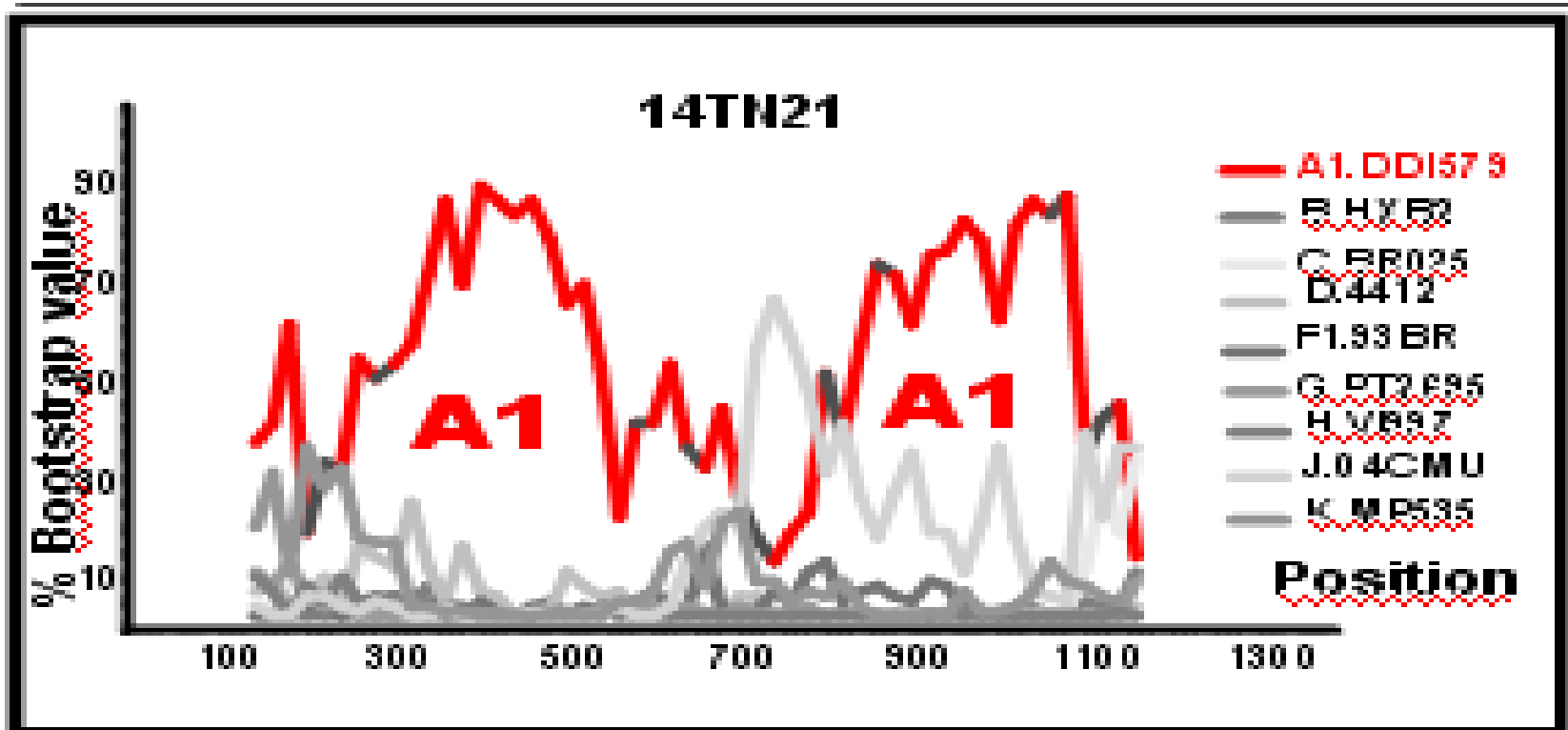
**Tunisian URF B/ D**



**Tunisian URF G/ B**

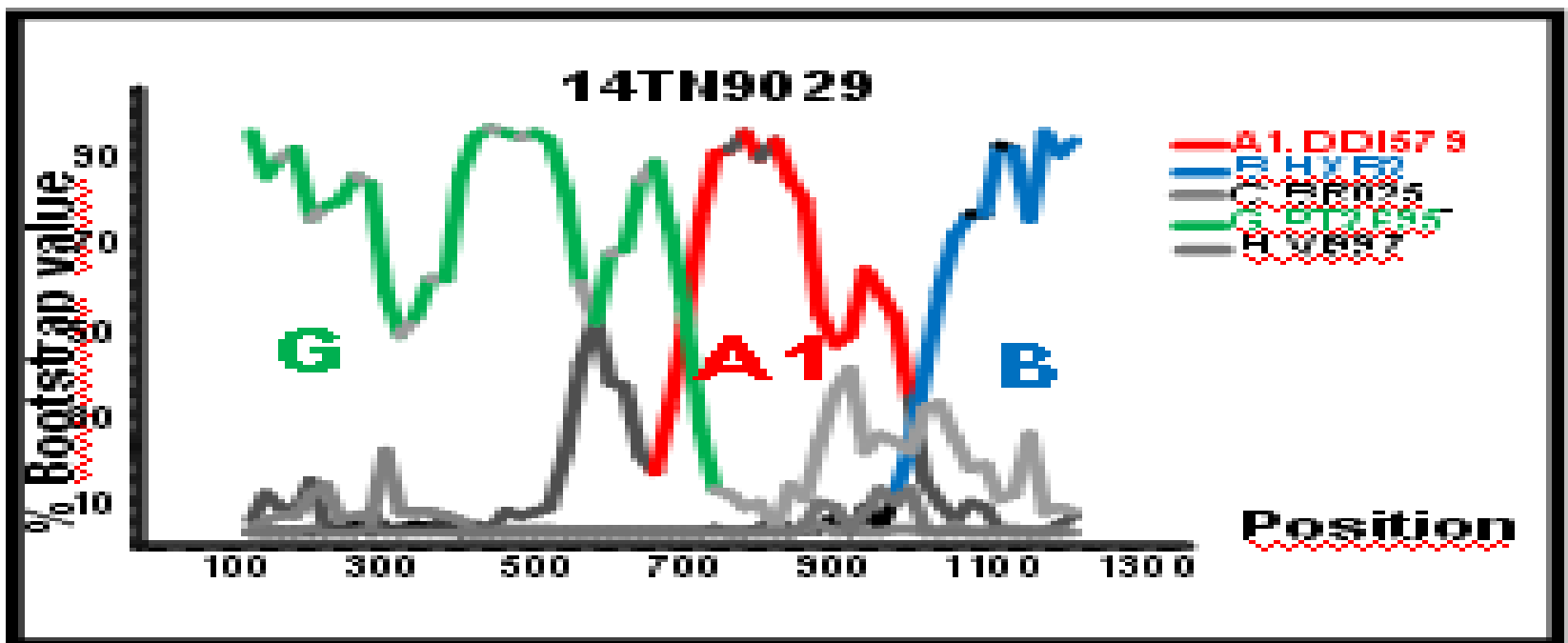


Tunisian URF **G/A1**

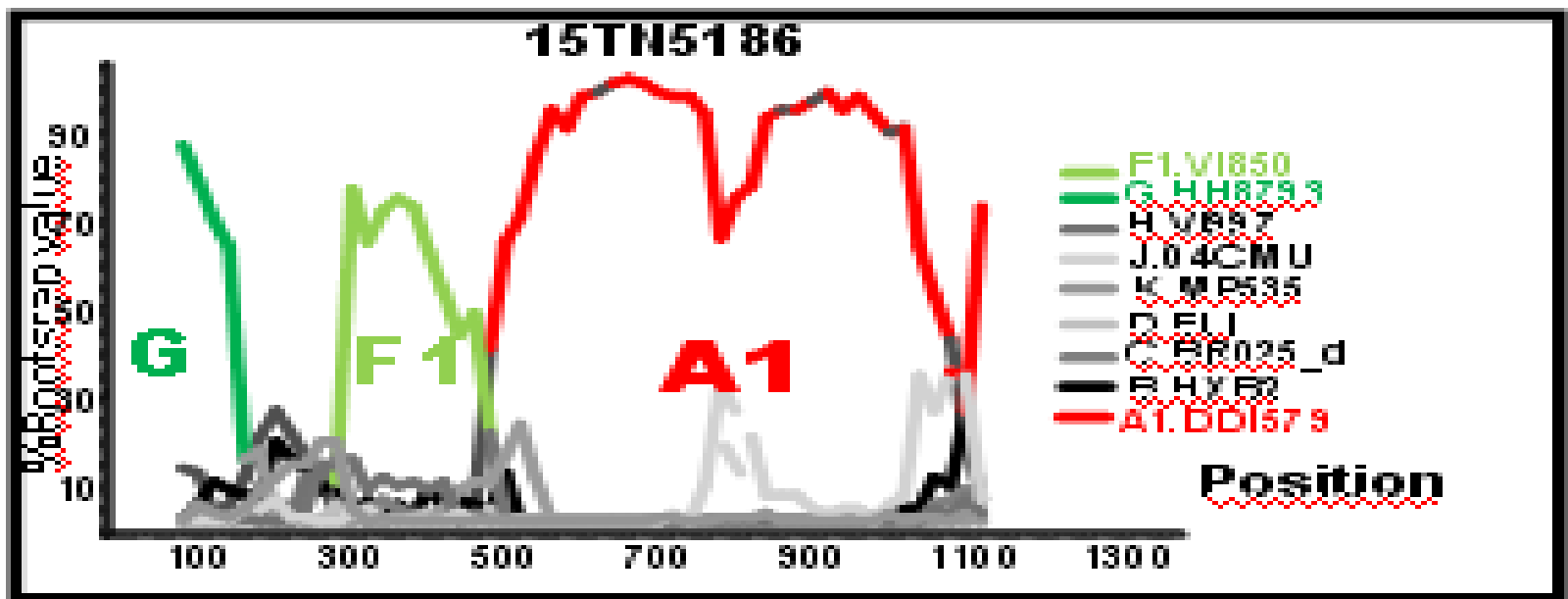


Tunisian URF **A1/U / A1**

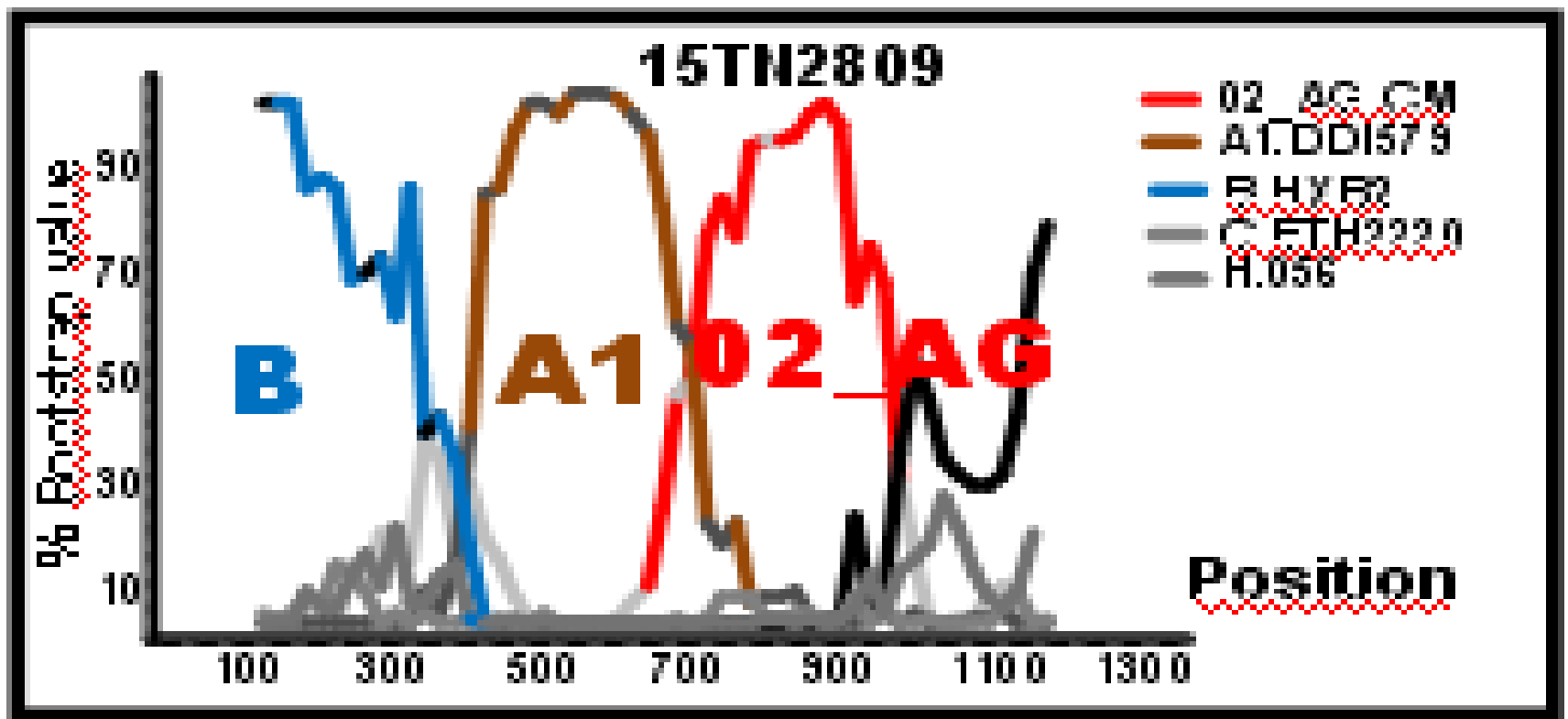




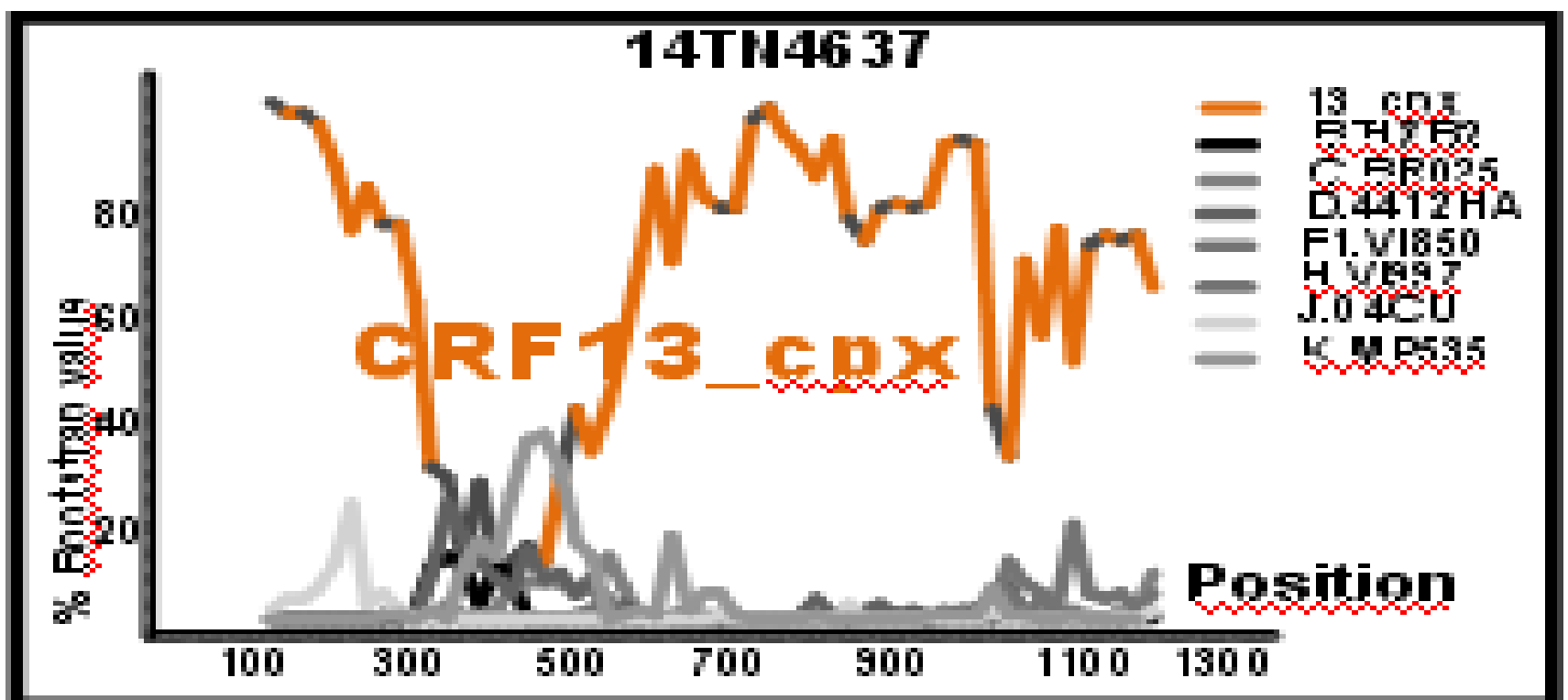
Tunisian URF **G** / **A1** / **B**



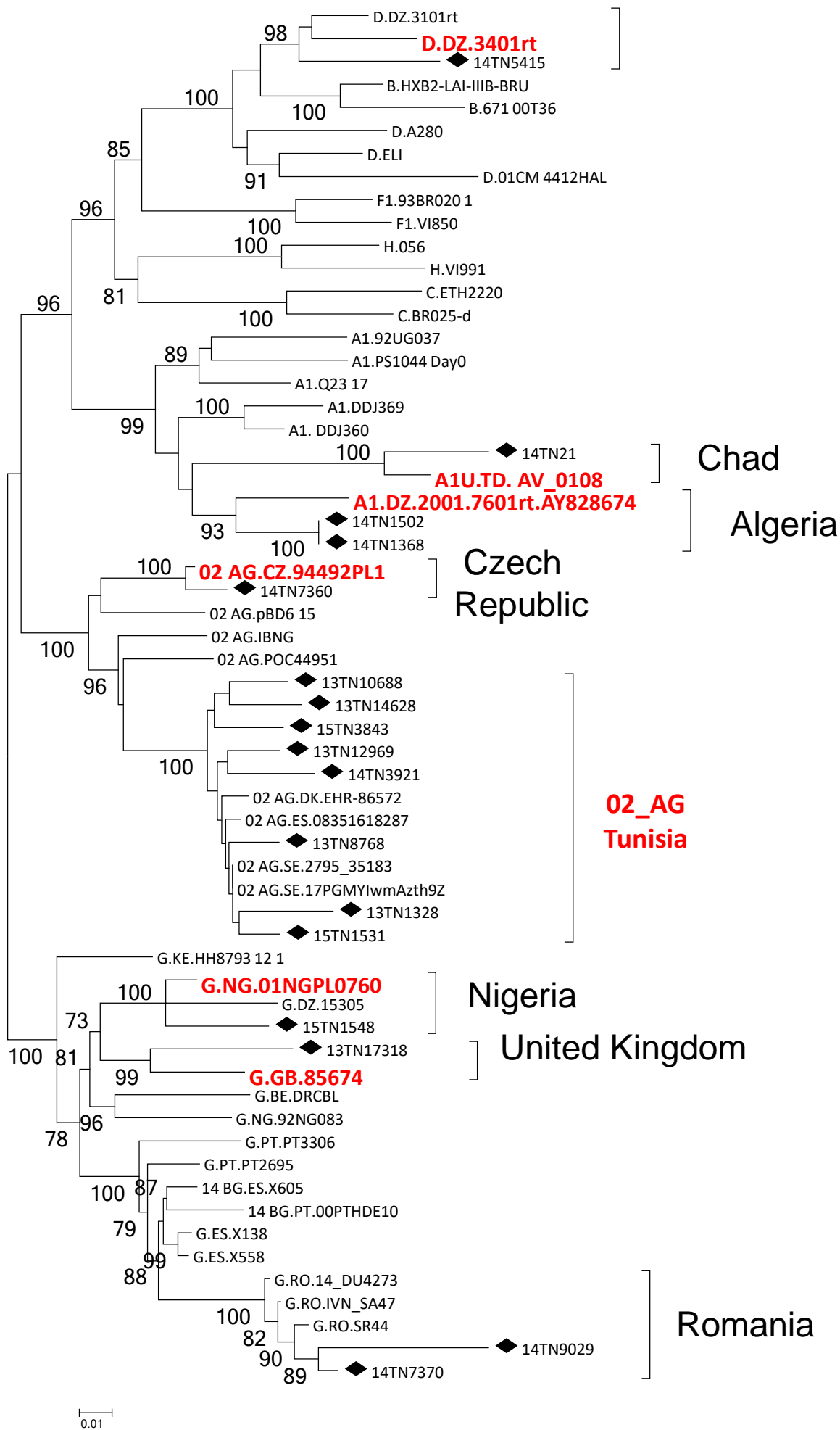
Tunisian URF **G** / **F1** / **A1**



Tunisian URF **B** / **A1** / **CRF02\_AG**



Tunisian URF **CRF13\_cpx** / **U** / **CRF13\_cpx**



**Phylogenetic tree showing the relationship between HIV-1 isolates from Tunisia and database viruses.**

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# AIDS Research and Human Retroviruses

Special Issue  
on HIV Cure Research

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This article has

## Genetic Diversity of HIV-1 in Tunisia

Awatef El Moussi<sup>1,2,3</sup>, Michael M. Thomson<sup>4</sup>, Elena Delgado<sup>4</sup>, Maria Teresa Cuevas<sup>4</sup>, Majda Nasr<sup>1</sup>, Salma Abid<sup>1,2</sup>, Mohamed Ali Ben Hadj Kacem<sup>1,2</sup>, Hanene Benaissa Tiouiri<sup>3</sup>, Amel Letaief<sup>6</sup>, Mohamed Chakroun<sup>7</sup>, Mounir Ben Jemaa<sup>8</sup>, Hayet Hamdoui<sup>3,9</sup>, Rafla Tej Dellagi<sup>9</sup>, Khaled Kheireddine<sup>3,10</sup>, Ilhem Boutiba<sup>1,2</sup>, Lucia Pérez-Álvarez<sup>4</sup>, and Amine Slim<sup>1,2</sup>

1-Unit Virology, Microbiology Laboratory, Charles Nicolle University Hospital, Tunis, Tunisia

2- Laboratory of Research “resistance to antibiotics” Faculty of Medicine of Tunis, Tunisia

3- The Global Fund to Fight AIDS, Tuberculosis and Malaria, Geneva, Switzerland

4-HIV Biology and Variability Unit, Centro Nacional de Microbiología, Instituto de Salud Carlos III, Majadahonda, Madrid, Spain

5- Infectious Diseases Department, Rabta University Hospital, Tunis, Tunisia

6- Infectious Diseases Department, Farhat Hached University Hospital, Sousse, Tunisia

7- Infectious Diseases Department, Fatouma Bourguiba University Hospital, Monastir, Tunisia

8- Infectious Diseases Department, Hedi Chaker University Hospital of Sfax, Sfax, Tunisia

9- Primary Health Care Directory (DSSB), Ministry of Health, Tunisia

10- National Office of Family and Population, Tunis, Tunisia

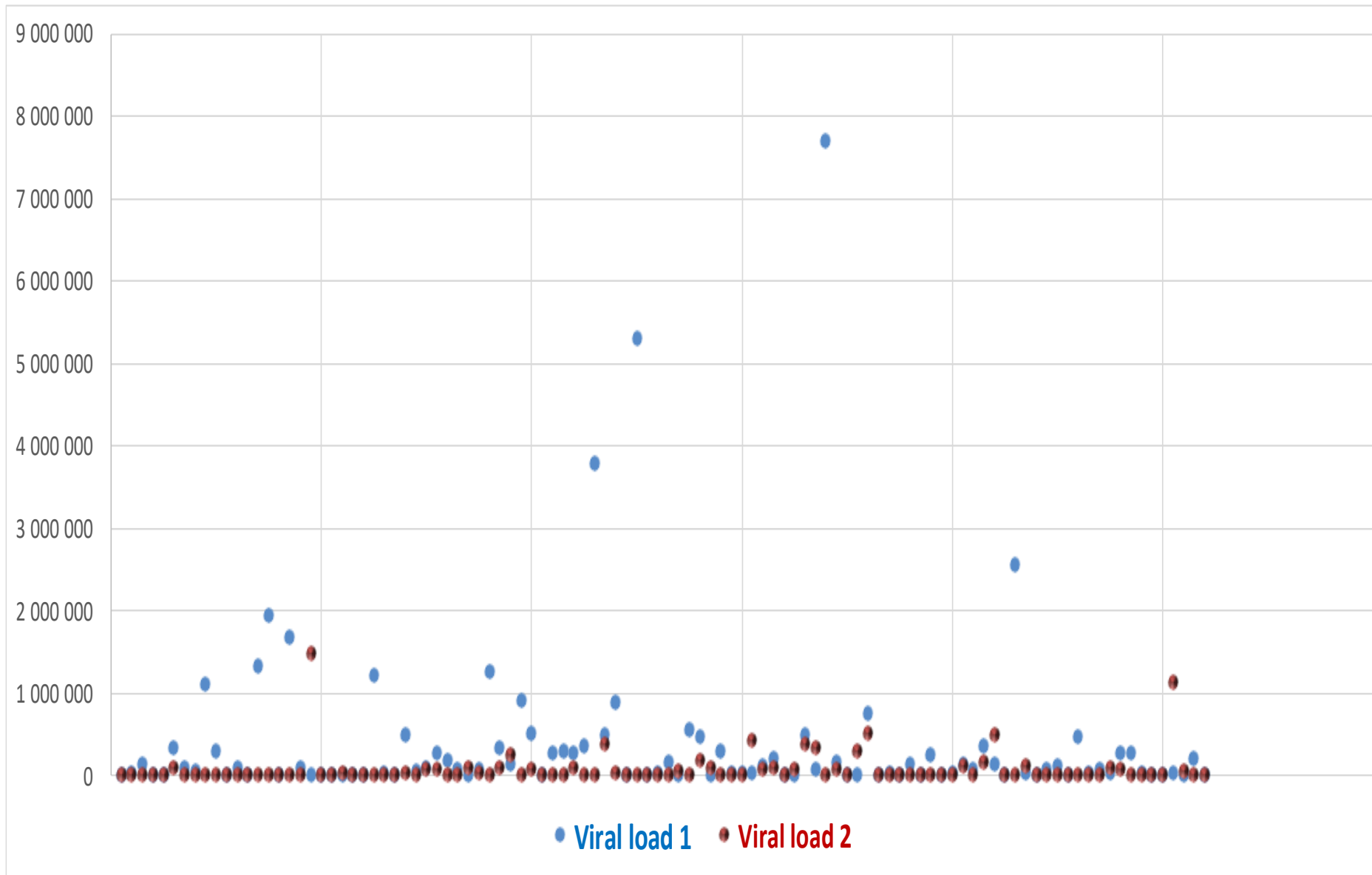
Corresponding author: Awatef El Moussi; Unit Virology, Microbiology Laboratory, Charles Nicolle University Hospital, Tunis, Tunisia.

Email: [awatefbio@gmail.com](mailto:awatefbio@gmail.com)

**Viral Load before and after Genotyping test**

Nbre	Sampling date 1	Viral load 1	Sampling date 2	Viral load 2	Difference
1	19/04/2014	3 750	19/07/2014	99	3 851
2	07/06/2014	32 922	03/08/2014	104	32 818
3	07/06/2014	141 482	14/03/2015	1470	140012
4	30/08/2014	2 955	29/11/2014	undetectable	2 955
5	31/05/2014	1 858	06/06/2015	44	1 806
6	24/05/2014	345 011	25/04/2015	98 800	147 411
7	03/05/2014	89 600	12/07/2014	762	88 838
8	21/06/2014	63 472	20/09/2014	12 600	50 872
9	14/05/2014	1 101 550	02/08/2014	922	1 100 628
10	05/07/2014	286 290	09/05/2015	950	285 340
11	28/06/2014	12 426	23/08/2014	82	12 344
12	12/07/2014	87 324	20/09/2014	386	86 938
13	21/06/2014	2 832	01/11/2014	undetectable	2 832
14	26/07/2014	1 320 000	31/01/2015	98	1 319 902
15	17/05/2014	1 941 277	28/06/2014	2736	1 938 541
16	05/07/2014	2 536	20/09/2014	10 600	
17	16/08/2014	1 679 909	16/05/2015	undetectable	1 679 909
18	10/05/2014	91 700	19/07/2014	924	90 776
19	12/07/2014	13 319	27/12/2014	1 490 000	
20	20/09/2014	7 450	25/04/2015	217	7 233
21	20/09/2014	>10 000 000	15/11/2014	4539	9 995 461
22	01/02/2014	12 900	19/04/2014	36 400	
23	20/09/2014	12 600	09/01/2016	undetectable	12 600
24	18/10/2014	1 623	18/04/2015	181	1 442
25	01/11/2014	1 219 603	29/11/2014	1296	1 218 307
26	01/11/2014	22 052	05/09/2015	3834	18 218
27	08/11/2014	>10 000 000	20/12/2014	20 459	9 979 541
28	08/04/2014	504 000	30/04/2016	31 100	472 400
29	19/04/2014	48 700	17/01/2015	93	48 607
30	07/06/2014	101 544	28/06/2014	65 251	36 293
31	31/05/2014	267 175	04/04/2015	75 400	551 775
32	05/04/2014	183 000	19/07/2014	300	182 700
33	24/05/2014	83 681	26/07/2014	488	7 880
34	28/06/2014	15 184	19/07/2014	94 700	
35	07/05/2014	66 159	18/10/2014	24 424	41 535
36	05/07/2014	1 256 098	30/08/2014	638	1 255 460
37	24/05/2014	345 011	25/04/2015	98 800	246 211
38	05/07/2014	143 451	10/01/2015	246 000	
39	05/07/2014	901 518	23/05/2015	97	901 421
40	12/07/2014	523 984	27/09/2014	75 500	448 484
41	28/06/2014	3 230	28/03/2015	477	2 753
42	12/07/2014	266 925	16/05/2015	<20	266 905
43	09/08/2014	303 814	27/09/2014	350	303 464
44	13/09/2014	270 587	24/10/2015	106 000	164 587
45	20/09/2014	368 000	04/04/2015	100	367 000
46	27/09/2014	3 780 000	20/12/2014	1645	3 778 377
47	01/02/2014	483 000	27/09/2014	385 000	98 000
48	07/02/2014	889 000	03/15/2014	23 957	865 043
49	06/09/2014	7 464	27/08/2016	18 000	
50	18/10/2014	5 312 953	07/03/2015	undetectable	5 312 953
51	21/10/2014	8 612	11/08/2016	12 400	
52	08/11/2014	26 325	23/04/2016	61	26 264
53	24/11/2014	159 043	04/04/2015	undetectable	159 043
54	25/11/2014	> 10 000 000	24/09/2016	58 692	9 941 308
55	15/11/2014	560 925	07/03/2015	60	560 865
56	01/11/2014	466 678	02/01/2016	190 000	276 678
57	15/11/2014	1368	28/11/2015	91 800	
58	13/12/2014	285 745	24/01/2015	1810	283 935
59	20/12/2014	21 700	28/03/2015	10 800	10 900
60	27/12/2014	37 000	22/10/2016	10 409	26 591
61	27/12/2014	40 500	01/08/2015	429 399	
62	11/01/2014	127 000	20/12/2014	79 600	47 400
63	25/01/2014	207 000	28/05/2014	87 223	119 777
64	29/01/2014	5 220	11/11/2015	4720	500
65	01/02/2014	12 900	19/04/2014	86 400	73 500
66	01/02/2014	483 000	27/09/2014	385 000	98 000
67	15/02/2014	67 200	15/11/2014	331 950	
68	15/02/2014	7 710 000	31/05/2014	2061	7 707 939
69	22/02/2014	155 000	31/05/2015	85 200	
70	22/02/2014	6 130	31/05/2014	8 556	
71	22/03/2014	6 930	05/08/2017	289 000	
72	25/03/2014	755 000	10/05/2014	515 000	240 000
73	29/03/2014	2 650	20/09/2014	7 450	
74	04/04/2014	27 000	04/02/2015	14 900	12 100
75	05/04/2014	871	23/04/2016	61	810
76	12/01/2015	140 000	10/10/2015	58	139 942
77	10/01/2015	3400	05/12/2015	84	3 316
78	10/01/2015	246 000	18/04/2015	76	245 924
79	17/01/2015	2 490	05/09/2015	449	2 041
80	17/01/2015	33 000	19/09/2015	<20	32 980
81	10/01/2015	136 000	10/02/2015	125 000	11 000
82	31/01/2015	85 200	11/04/2015	2 360	82 840
83	01/01/2015	356 000	27/02/2016	155 000	201 000
84	31/01/2015	149 000	08/04/2017	486 760	
85	31/01/2015	5 740	27/06/2015	119	5 621
86	31/01/2015	2 570 000	23/05/2015	49	2 569 951
87	10/01/2015	21 900	18/06/2016	112 000	
88	07/03/2015	17 200	02/05/2015	11 900	5 300
89	31/01/2015	81 500	12/12/2015	47	81 453
90	12/03/2015	120 000	14/05/2015	17 300	102 700
91	14/03/2015	1 470	18/04/2015	7630	
92	28/03/2015	477 000	15/08/2015	63	476 937
93	01/04/2015	30 700	29/08/2015	<40	30 660
94	02/03/2015	77 600	16/05/2015	909	76 691
95	18/04/2015	24 200	27/05/2016	105 000	
96	18/04/2015	267 000	11/07/2015	73 700	193 300
97	11/04/2015	284 000	01/08/2015	1467	282 533
98	11/04/2015	27 100	08/08/2015	12 539	14 561
99	18/04/2015	6950	01/08/2015	3500	3 450
100	18/04/2015	1370	05/09/2015	449	921
101	09/05/2015	38 100	15/08/2015	1 130 000	
102	09/05/2015	8 950	15/08/2015	48 525	
103	25/04/2015	202 000	05/03/2016	19 300	182 700
104	02/05/2015	3 310	22/08/2015	<40	3 270

# Viral load before and after genotyping test



- Viral load is reduced in **78 %** of these patients treated after genotyping test,
- **58 %** < 1000 copies/ ml,
- **22%** indicate “virological failure”,

# DRUG RESISTANCE IN TUNISIA





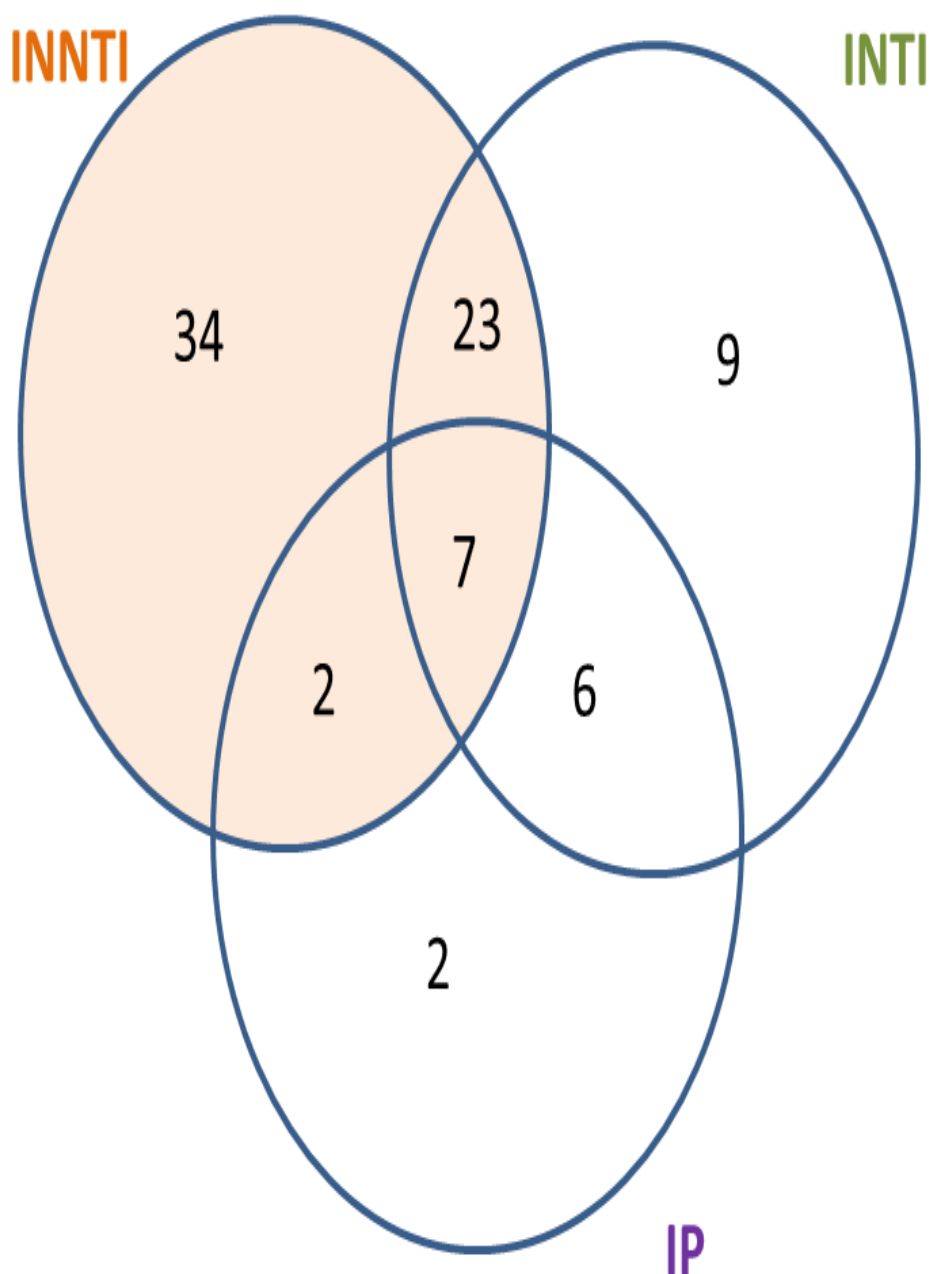
- We included **176** patients.
- Of these, **102** (57.9%) were **men** and **74** (42.1%) were **women**.
- **104** (59.1%) received antiretroviral treatment and **71** (40.3%) were naïve.



Sequences with SDRMs			
SequenceID	NRTI SDRMs	NNRTI SDRMs	PI SDRMs
13TN12396	None	<b>K103N</b>	None
13TN12968	None	<b>K103N</b>	None
13TN1328	<b>F77L</b>	None	None
13TN14619	<b>M184V</b>	<b>K103N, P225H</b>	None
13TN14620	<b>M184V</b>	<b>K103N, P225H</b>	None
13TN14624	None	None	<b>L90M</b>
13TN14625	<b>M41L, M184V, L210W, T215Y</b>	<b>K103S, G190A</b>	<b>M46L, I54V, G73A, V82A, L90M</b>
13TN15517	<b>M41L, L210W, T215Y</b>	None	<b>M46I, I50L, V82A, L90M</b>
13TN15820	<b>M184V</b>	<b>K101E, Y181C</b>	None
13TN1718	<b>M41L, D67N, T69D, K70R, T215F, K219Q</b>	<b>Y188L</b>	<b>M46I, I47V, I50V, L76V, V82F</b>
13TN7497	None	<b>L100I, K103N, P225H</b>	None
13TN8496	None	<b>K103N</b>	None
14TN10108	None	<b>G190S</b>	None
14TN10393	<b>L74IV, Y115F, M184V</b>	<b>K103N, P225H</b>	None
14TN10395	<b>M184V, T215Y</b>	<b>Y188HL</b>	None
14TN10403	None	<b>K103N</b>	None
14TN1048	<b>M184V</b>	None	None
14TN10767	None	<b>K103N, P225H</b>	None
14TN11141	<b>L74IV, Y115F, M184V</b>	<b>K103N, P225H</b>	None
14TN11630	<b>L74V, M184V</b>	<b>K103N, P225H</b>	None
14TN11643	<b>M184V</b>	<b>V106M, G190A</b>	None
14TN11745	<b>M184V</b>	None	None
14TN1186	<b>L74V, M184V</b>	<b>L100I, K103N</b>	None
14TN12297	<b>K65R, L74I, K219N</b>	<b>K103N, Y181C, P225H</b>	<b>M46I, F53L, I54V, L76V, I84V</b>
14TN12494	<b>M41L, V75M, F77L, M184V, L210W, T215Y</b>	None	<b>M46I, I54V, V82F, L90M</b>
14TN1272	<b>M184V</b>	None	<b>M46I, I50V, I54V, V82F</b>
14TN12946	<b>L74IV, Y115F, M184V</b>	<b>K103N, P225H</b>	None
14TN12954	None	<b>K103N</b>	None
14TN13313	None	<b>K103N</b>	None
14TN13941	<b>K65R</b>	None	None
14TN14890	<b>D67N, K70R, M184V, K219Q</b>	<b>K103N, P225H</b>	<b>V32I, M46I, I47V, V82A, I84V</b>
14TN1491	<b>K65R, M184V</b>	<b>K103N, V106M</b>	None
14TN1660	<b>M41L, M184V, T215F</b>	None	None
14TN1701	<b>D67N, K70R, T215F, K219Q</b>	<b>K101P, K103S</b>	<b>V32I, M46I, I54L, L76V, L90M</b>
14TN1809	None	<b>K103N</b>	None
14TN1831	<b>K219Q</b>	None	None
14TN188	None	<b>K103N</b>	None
14TN2174	<b>M184V</b>	<b>K101E, Y181C</b>	None
14TN2721	<b>K70R, M184V, T215I, K219Q</b>	<b>K103N, M230L</b>	None
14TN3341	<b>M184V</b>	None	None
14TN3431	<b>T215F</b>	None	None
14TN3562	<b>M184V</b>	<b>K103N, P225H</b>	None
14TN3644	None	<b>K103N, G190A, P225H</b>	None
14TN384	None	<b>K103N</b>	None
14TN5419	None	<b>K103N, P225H</b>	None
14TN6031	<b>M184V</b>	<b>K103N, P225H</b>	None
14TN7101	<b>M184V</b>	None	None
14TN754	<b>M184V</b>	<b>K103N</b>	None
14TN7628	<b>M41L, D67N, T69D, K70R, T215F, K219Q</b>	<b>Y188L</b>	<b>M46I, I47V, I50V, L76V, V82F, L90M</b>
14TN8191	None	<b>K103N</b>	None
14TN9310	None	<b>K103N</b>	None
14TN9872	<b>L74V, Y115F, M184V, K219E</b>	<b>L100I, K103N</b>	None
15TN1538	None	<b>K103N</b>	None
15TN1544	<b>M41L, V75M, M184V, L210W, T215Y</b>	<b>K103N</b>	None
15TN1662	<b>D67N, K70R, M184V, T215F, K219E</b>	None	<b>L23I, M46L, I54V, V82A</b>
15TN1677	<b>D67N, K70R, M184V, K219Q</b>	None	<b>M46I, I54V, L76V, V82A</b>
15TN402	<b>M41L, V75M, M184V, L210W, T215Y</b>	None	<b>M46I, I54V, V82A, L90M</b>
15TN403	<b>L74I</b>	<b>K103N, P225H</b>	None
15TN409	None	<b>K103N</b>	None
15TN423	<b>D67G, T69D, K70R, T215F, K219Q</b>	<b>K103N, G190A</b>	None
15TN5177	None	<b>K103N, P225H</b>	None
15TN5596	None	<b>K103N</b>	<b>M46L, V82T, L90M</b>
15TN5597	<b>F77L, Y115F, F116Y</b>	None	None
15TN5599	<b>M41L, K70R, M184V, T215F, K219Q</b>	<b>K103N</b>	<b>V32I, M46I, I54L, L76V, I84V</b>
15TN5958	<b>M41L, M184V, L210W, T215Y, K219R</b>	<b>K103N, M230L</b>	None
15TN6136	None	<b>K103N</b>	None
15TN6488	<b>M184V</b>	<b>K103N</b>	None
15TN6500	<b>M184V, T215SY</b>	<b>Y188HL</b>	None
15TN6690	None	<b>K103N</b>	None
15TN6730	<b>M184V</b>	None	None

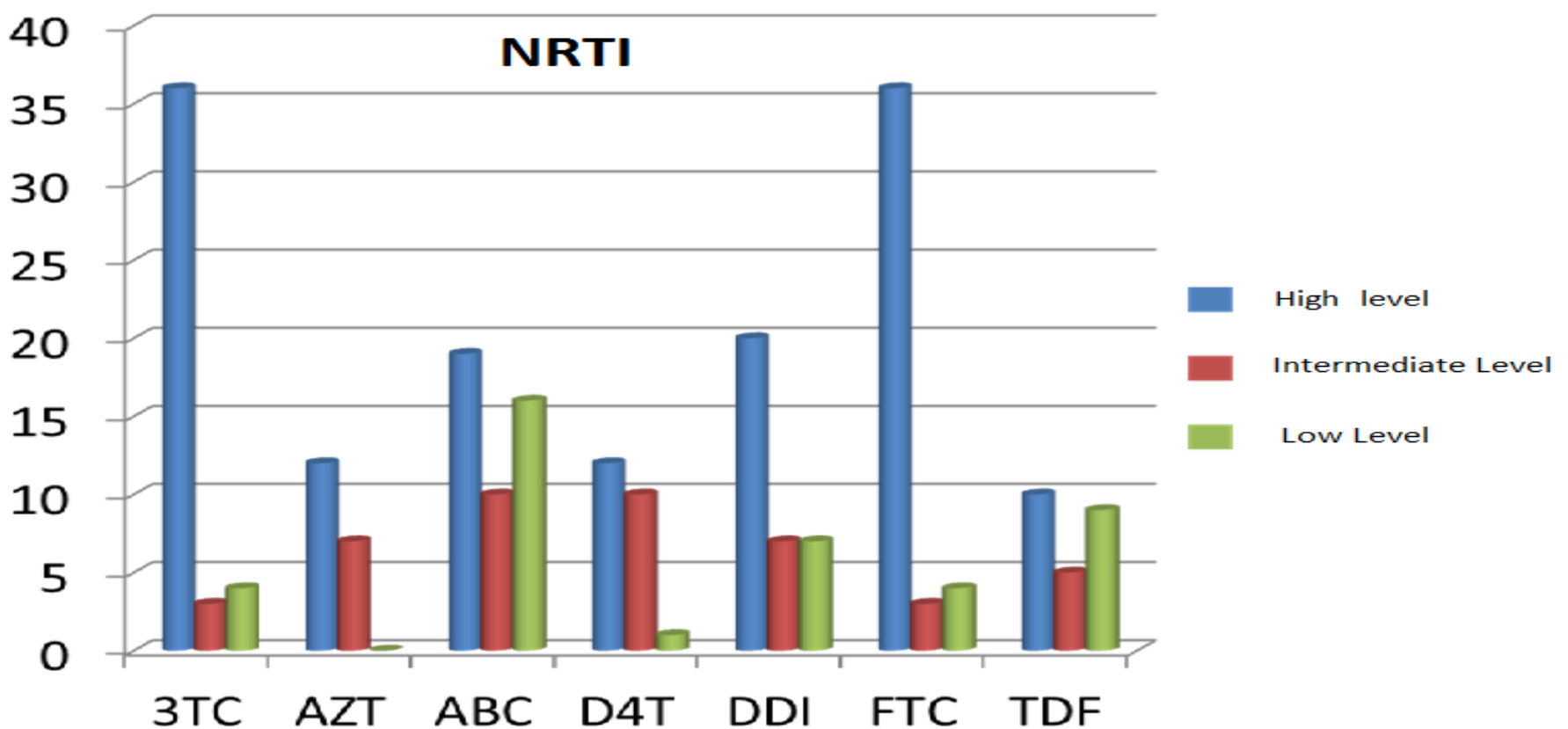
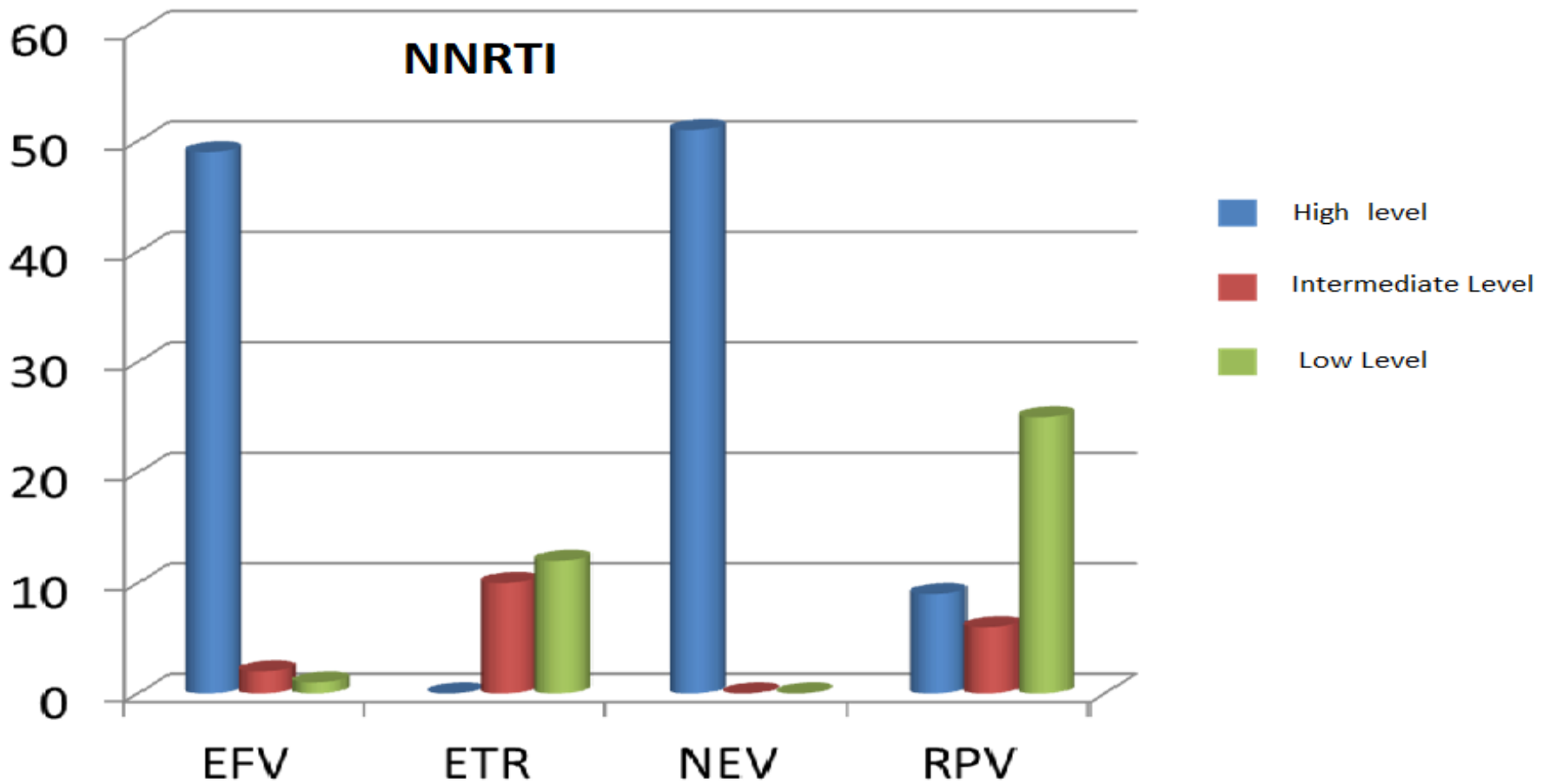
- 83 (47.2%) patients had antiretroviral resistance.
- Of these, 71 (85.6%) were treated patients and 12 (14.4%) were naïve patients,

# Distribution of resistance to different classes of drugs

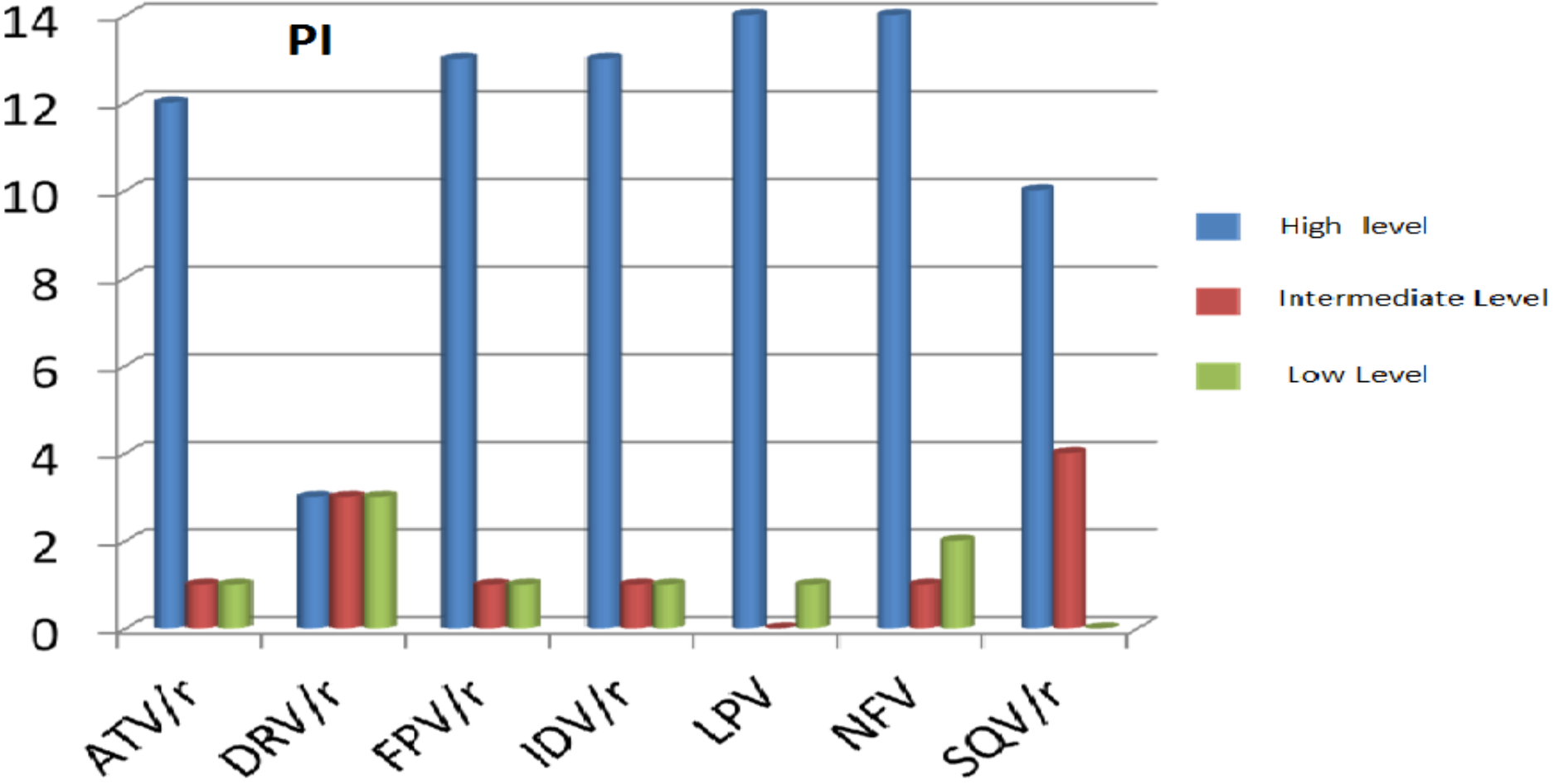


- 45 (54.2%) patients are resistant to **1** class of drugs: **9** to NRTI, **34** to NNRTI and **2** to IPs.
- 31 (37.4%) patients are resistant to **2** classes: **23** to NRTI + NNRTI **6** to NRTI + IP and **2** to NNRTI + IP.
- 7 (8.4%) patients are resistant to **3** classes,
- From the total of **71** naïve patients, **12** (16.9%) presented resistance,
- From them 10 to **NNRTI** (7 E138A/Q), **1** to IP and **1** to NRTI + IP

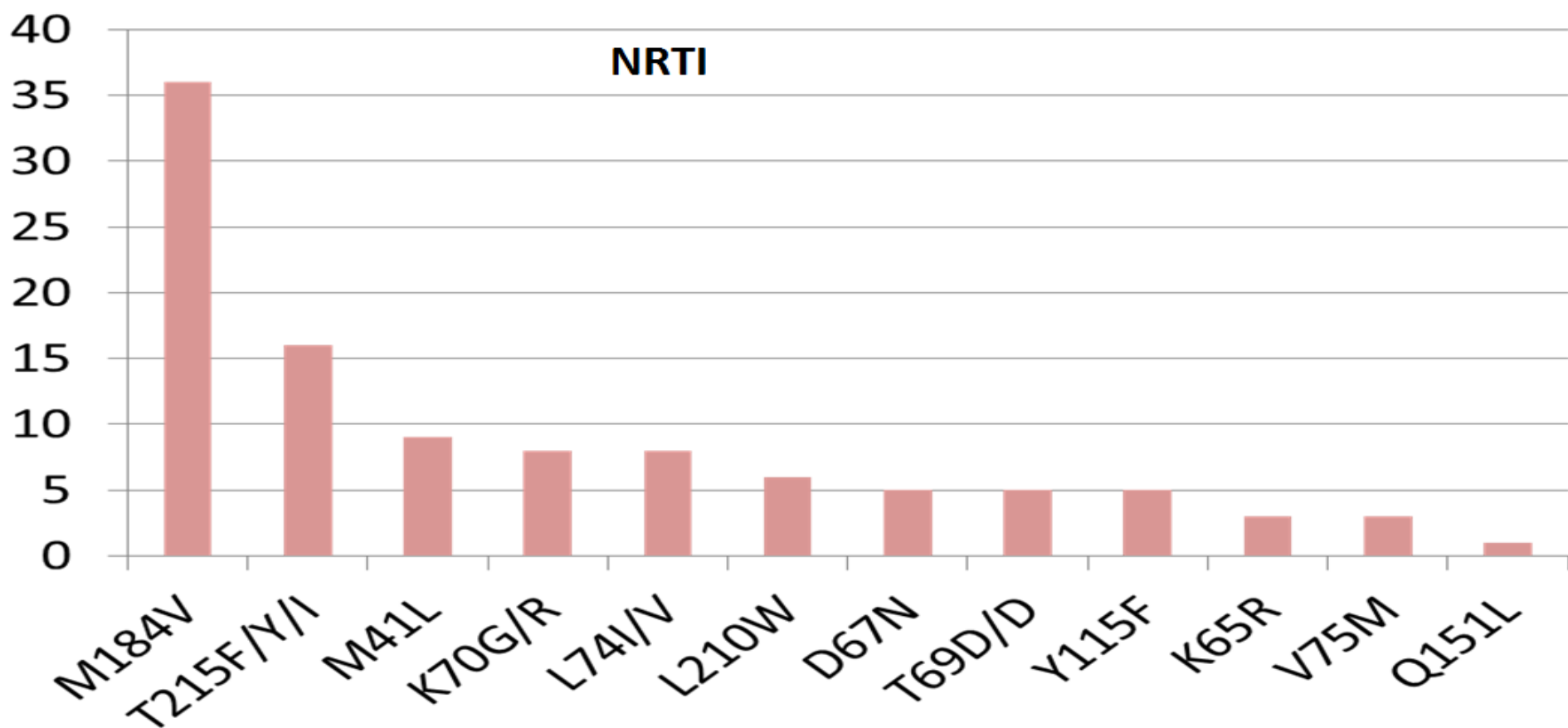
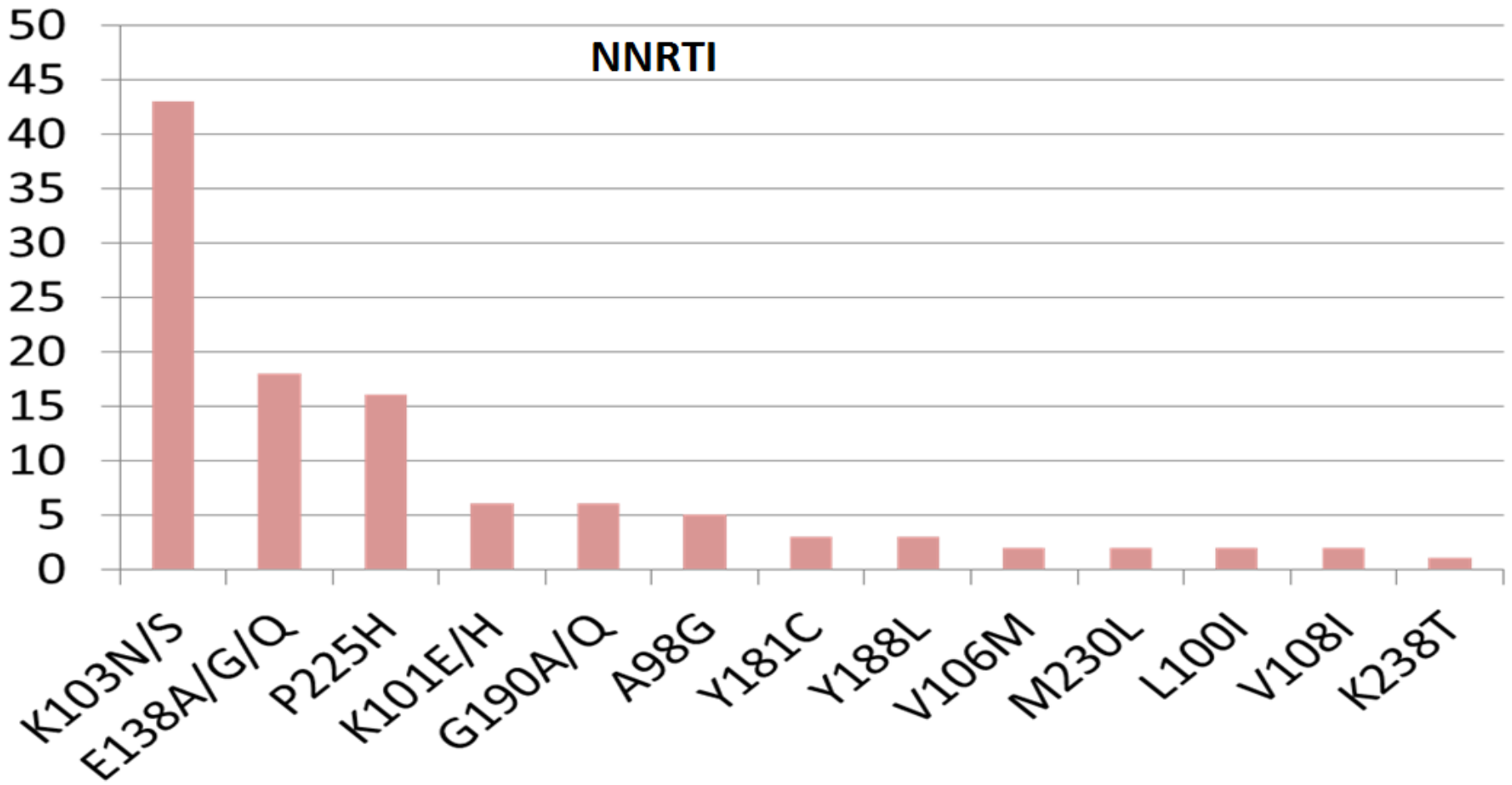
# Frequency and level of resistance to each drug



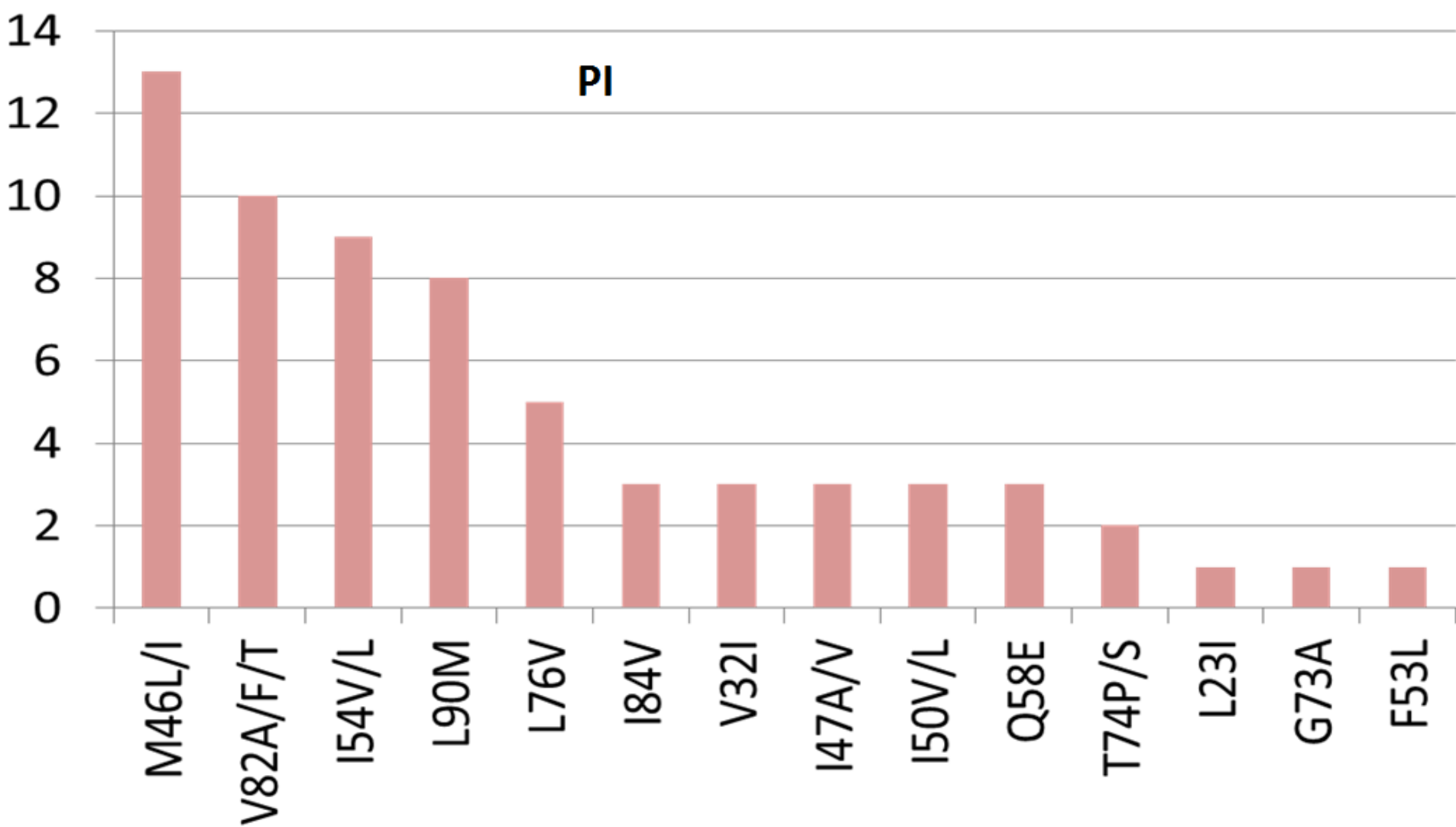
**PI**



# Frequency of antiretroviral resistance mutations



# Frequency of antiretroviral resistance mutations



# Conclusion

- We observed a **high level of Drug resistance** in ARV-treated patients and a **high prevalence of resistance in naïve patients** is described for the first time.
- Many patients have mutations of resistance to more than one class of drugs, so it would be better to introduce other classes of drugs, such as **integrase inhibitors** or **inhibitor of the entry of the virus**,
- The **great diversity of HIV-1 genetic forms** detected in this study reflects the impact of migration from West Africa to Tunisia as a transit country for subsequent migration to Europe.
- Highlight the need to promote **surveillance** studies on HIV genetic diversity and the emerging of new resistance to the drugs in this region.





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