

High rates of primary resistance to NNRTI among patients with HIV-1 non-B clades infection from Lausanne

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Introduction

Data concerning HIV-1 primary resistance to HAART mainly rely on studies performed in chronic infected patients.

In Europe

JID 2005, CATCH study (n=2208)

Reports 10.4% prevalence of **related resistance mutations** mainly among subtype B (70%) chronic and newly infected naïve patients.

Introduction.2

The Swiss HIV Cohort Study

AIDS 2001, (n=197)

Primary drug resistance was identified in 8.6% of the PHI due to subtype B (74% of the cases).

Arch Intern Med 2007, (n=1812)

Primary drug resistance was found in 5% of chronic naïve patients (n=112/1812)

Subtype B was detected in ~ 60% of patients with treatment failure (n=177/1812)

Objective

To investigate the current trends of HIV subtypes and antiretroviral drug resistance present among HIV-1 primary infected patients naïve to treatment from Lausanne.

Patients inclusion criteria

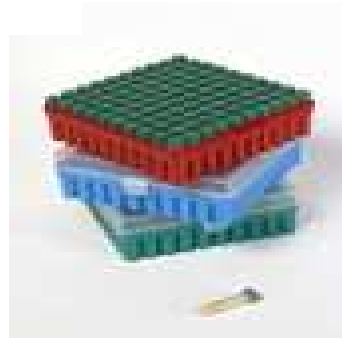
1. Enrollment during 2-3 weeks of onset of HIV primary infection symptoms.
2. Western blot incomplete seroconversion status.
3. Positive p24 antigen (ECL, Roche).

Clinical samples workflow

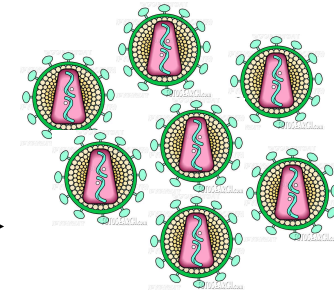
Day 0



Plasma



Viral
RNA



Virco® based
cDNA synthesis
and PCR



1497 bp

pol

Pr 1-99

RT 1-399

Computational analysis resources and sequence databases

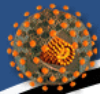
KATHOLIEKE UNIVERSITEIT
LEUVEN



REGA HIV Subtyping Tool

HIV BIOINFORMATICS
BIOAFRICA

<http://www.bioafrica.net/subtypetool/html/>



HIV Blast Los Alamos Database

<http://www.hiv.lanl.gov/content/hiv-db/>

HIVdb ▶ Genotype
PROGRAM Resistance
Interpretation

<http://hivdb.stanford.edu/>

Other algorithms:

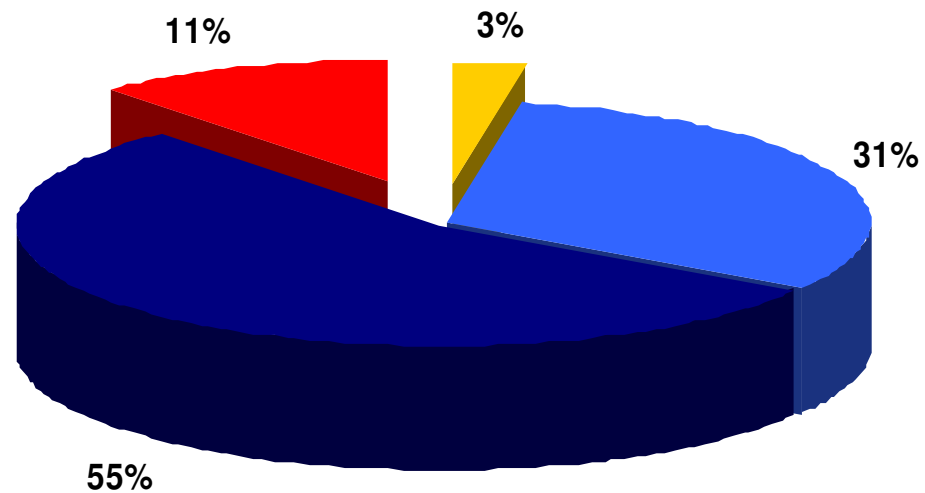
ANRS

IAS –USA Drug Mutation List,2006

Epidemiologic features

94% men

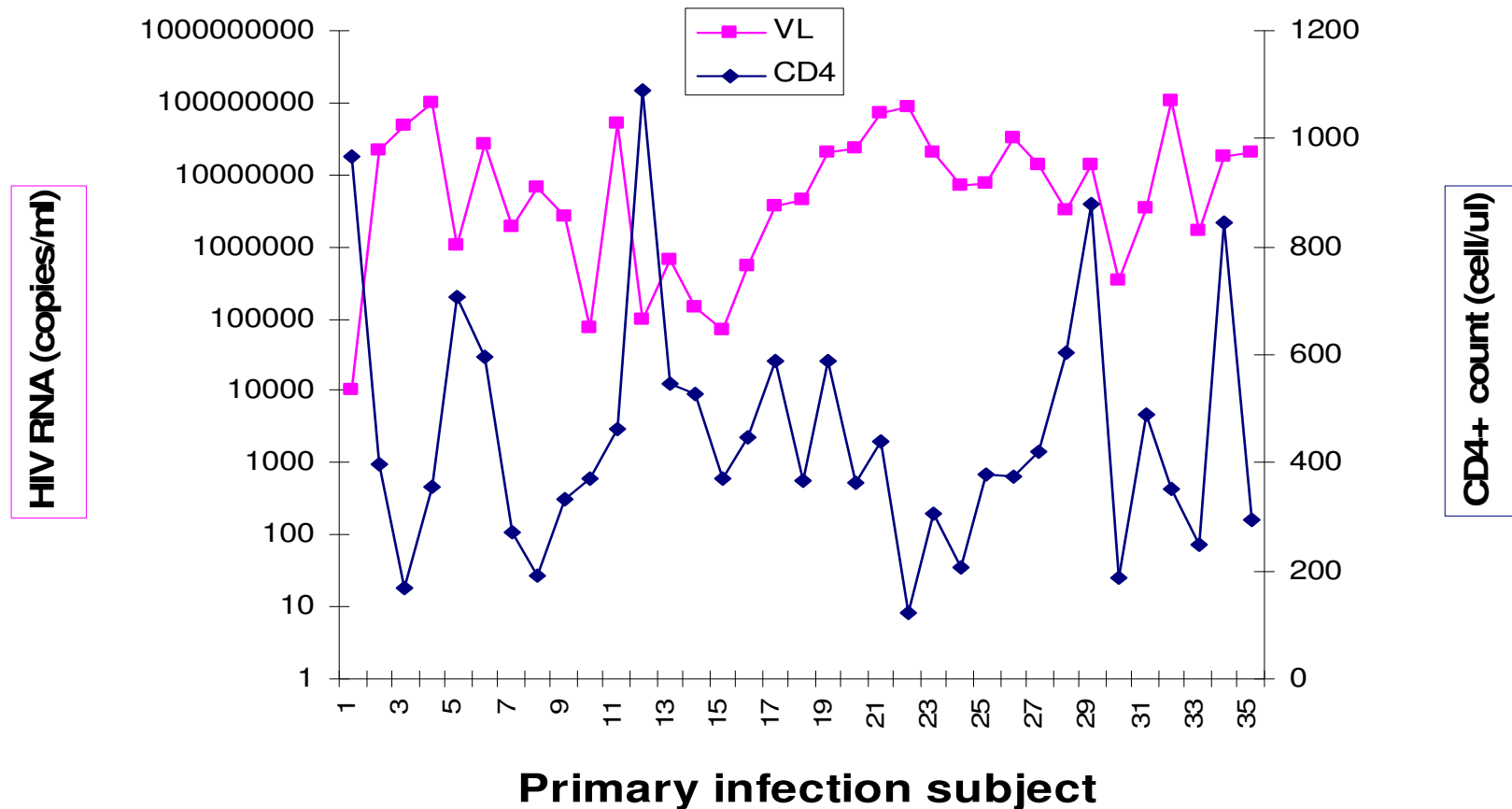
86% Sexual transmission route



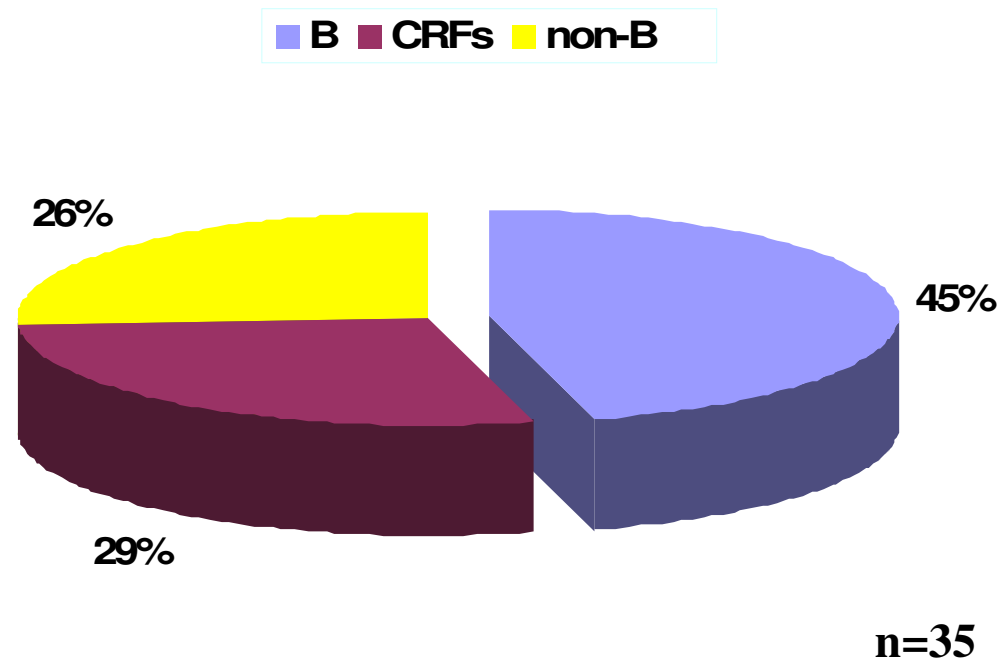
n=35

■ ND ■ HT ■ MSM ■ IV

HIV Viral load and CD4 counts at blood draw timepoint



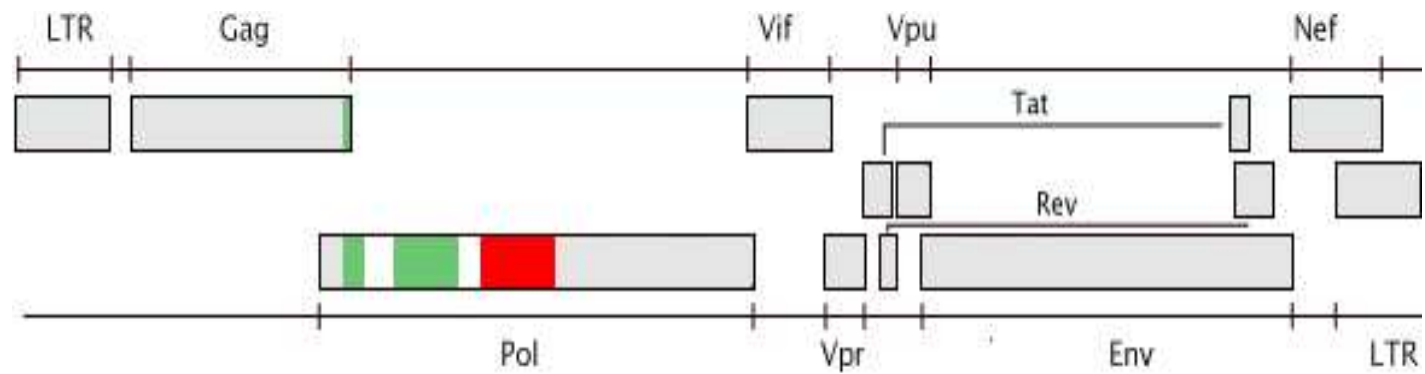
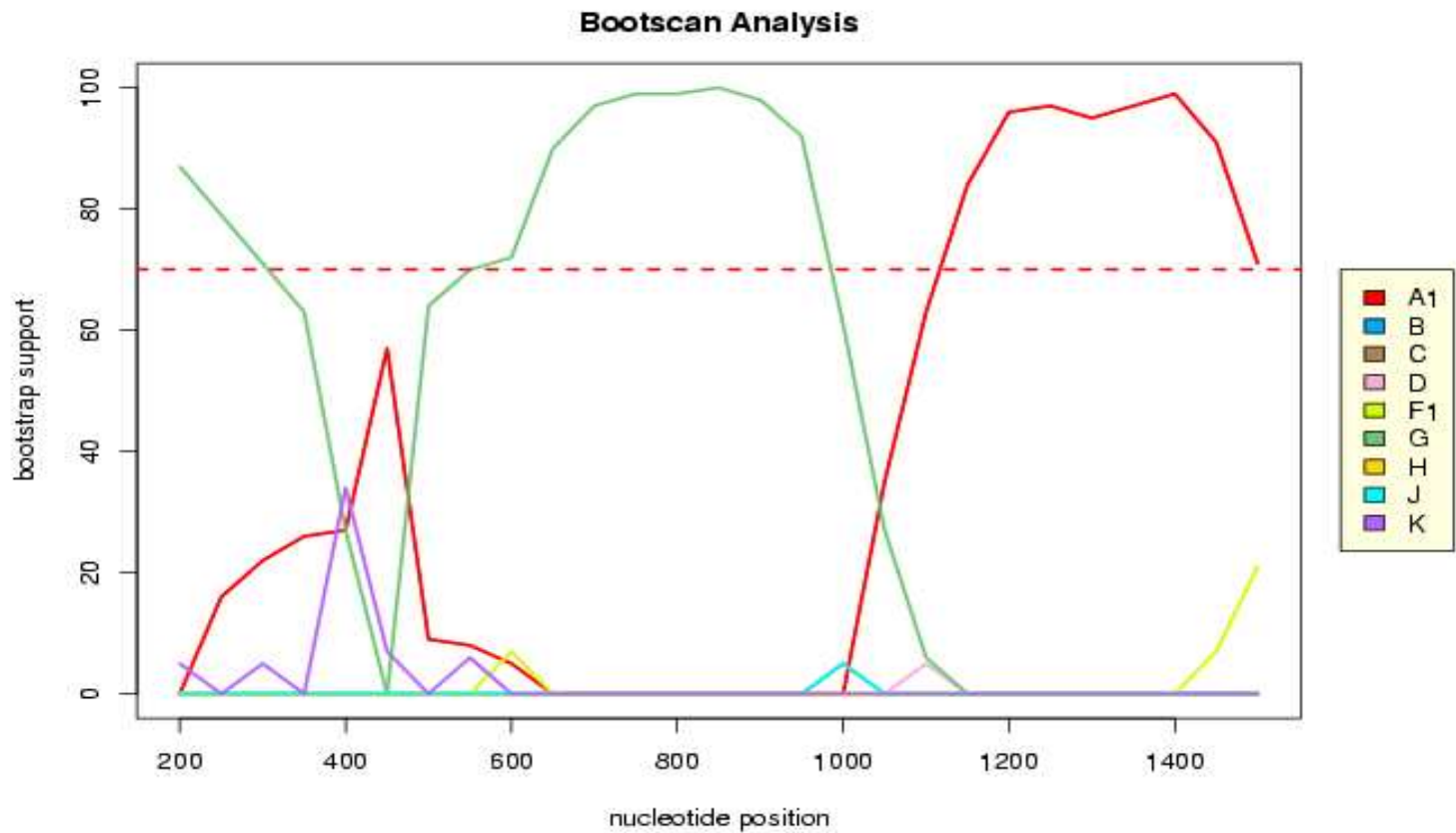
HIV Clade distribution



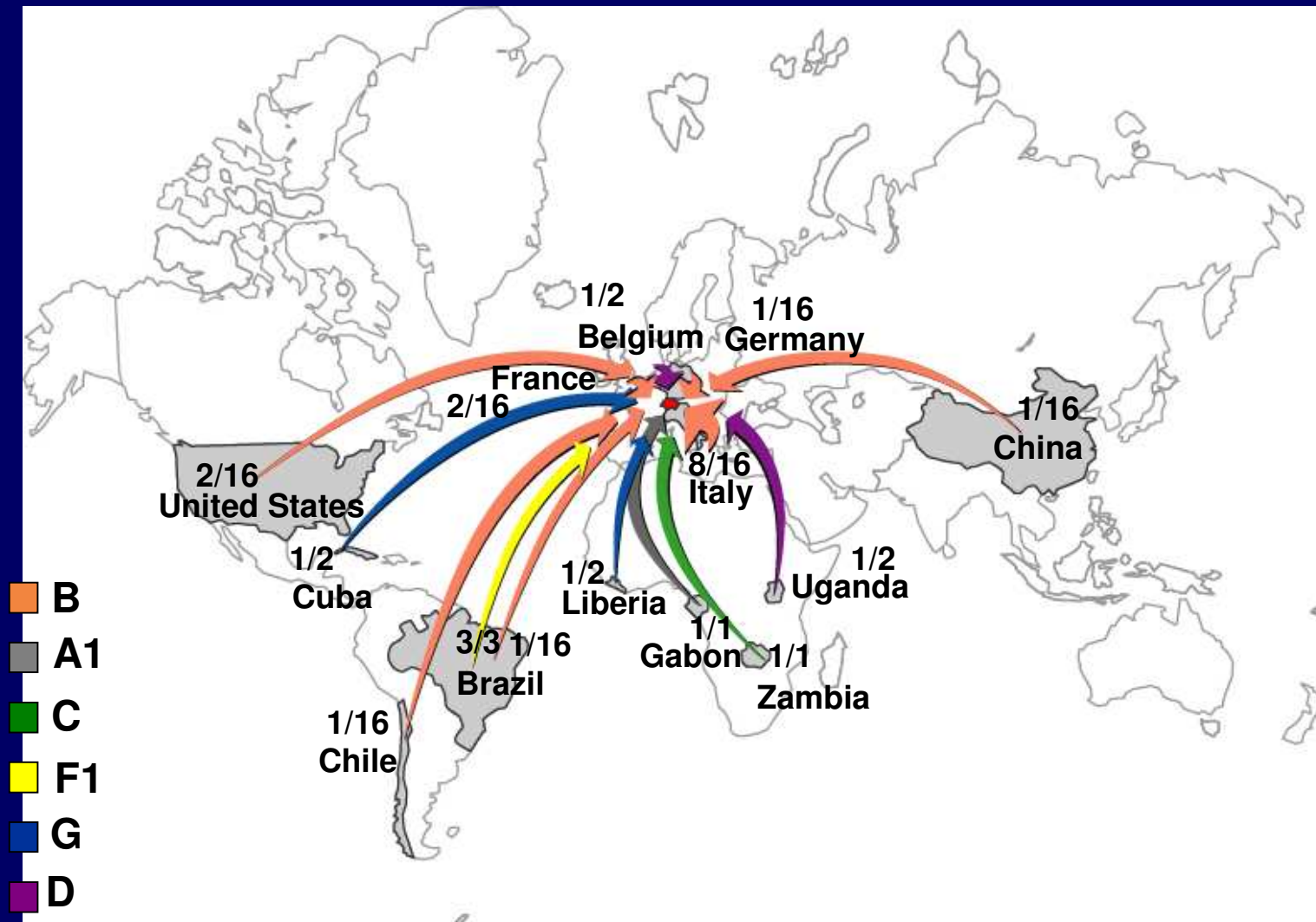
Bootscan analysis of pol 1.4kb

PHI 32

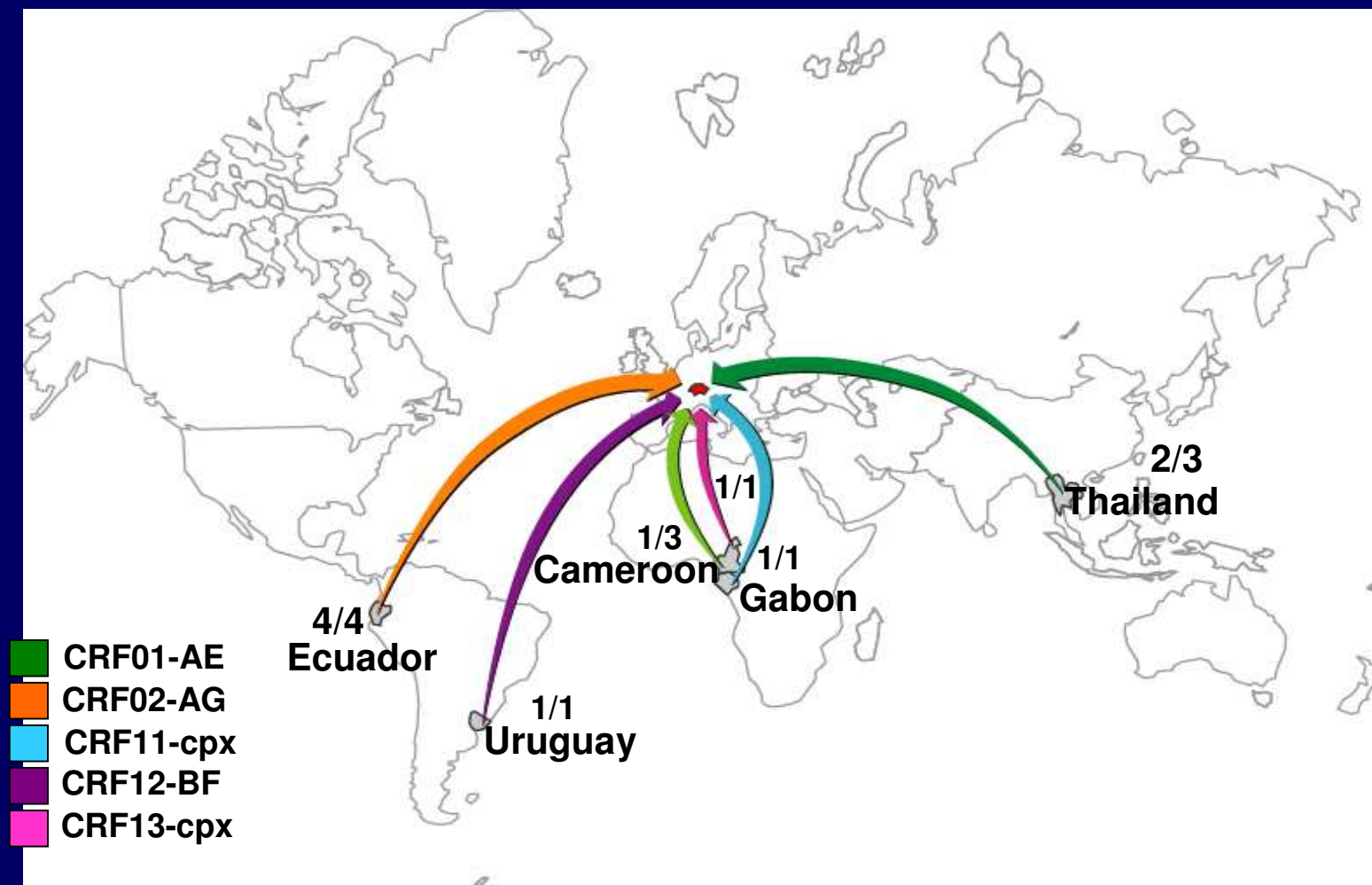
CRF02_AG 100% bootstrap



Blasting networks of HIV-1 group M subtypes harbored by primary infected individuals from Lausanne



Blasting networks of HIV-1 CRFs harbored by primary infected individuals from Lausanne



Resistance Mutations Screening

PI

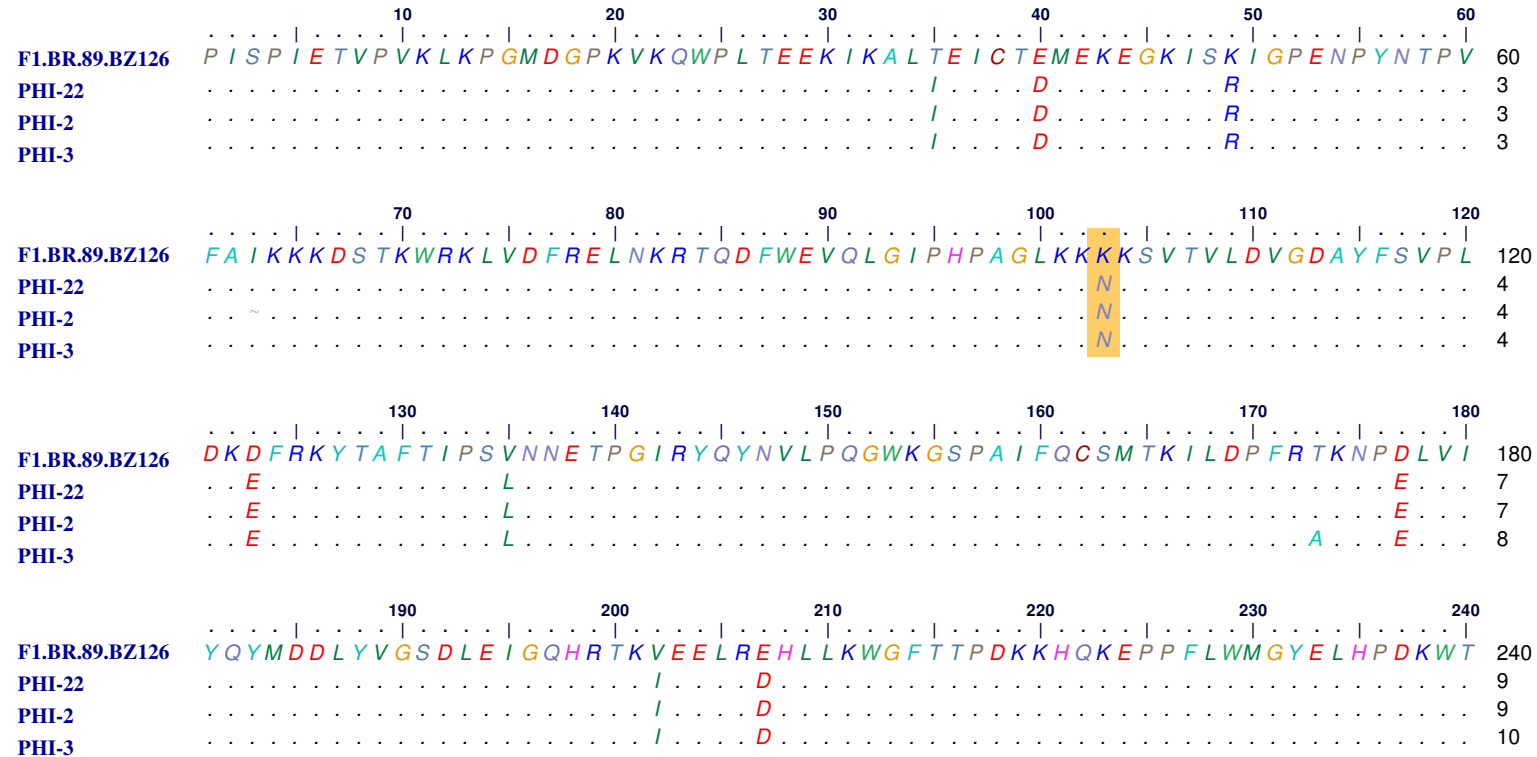
No major resistance mutation was identified.

RTI

Overall 4/35 patients harbored resistant viruses (11.4%) to NNRTI (4/4) and to NRTI (1/4).

Resistant strains corresponded to clades F1 (3/3) and D (1/2).

HIV-1 RT alignment of clade F1 sequences from the study

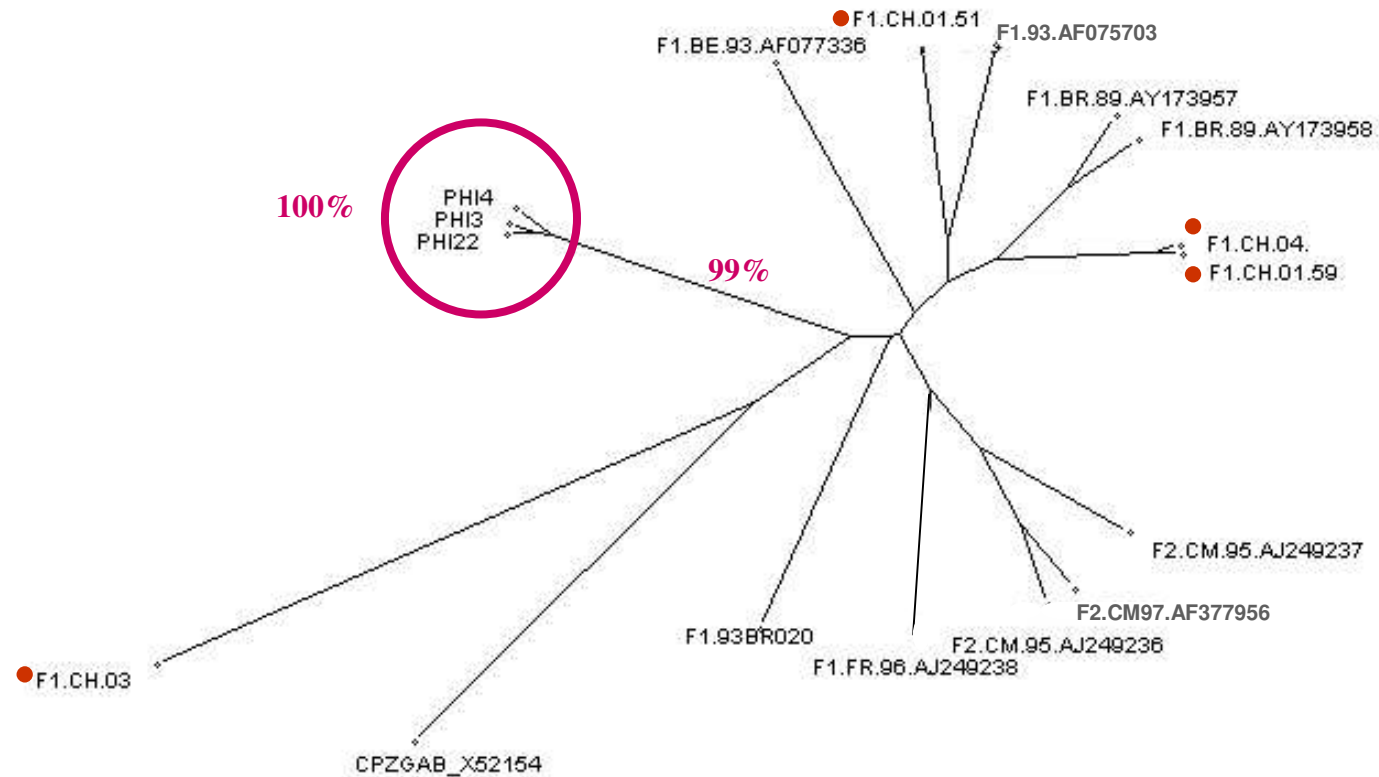


■ NNRTI drug resistance mutation 103N

Neighbor-joining tree of clade F1 sequences from the study

0.01

Pol alignment of PHI3, 4 and 22 to clade F1 and F2 reference sequences. Bootstrap resampling was performed 100 times .



HIV-1 RT alignment of all sequences with RTI resistance mutations from the study

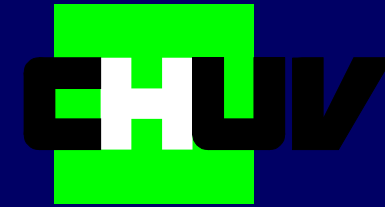


■ NNRTI drug resistance mutation 103N
■ TAMs 41L and 215Y

Conclusions

1. We identified a high rate of primary drug resistance among non-B strains (25%).
2. Mutation 103N was present in all resistant viruses, suggesting its cross-clade current transmission in the local epidemic.
3. These findings have relevant implications for future HAART surveillance studies in neighbor settings with similar phylogenetic networks.

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HIV analysis module