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HIV-1 pol gene diversity and archived nevirapine resistance mutation in pregnant women in rwanda

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Background

- This study aimed to find out whether genetic polymorphism was present in non-B subtypes from HIV-1 infected patients in Rwanda, especially in positions potentially affecting susceptibility to antiretroviral agents.
- A second objective was to look for appearance of NNRTI resistance mutations after a single dose of Nevirapine in PMTCT.

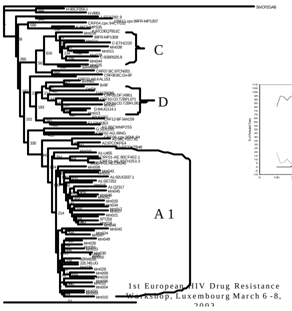
Methods

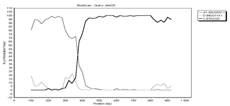
- Viral *pol* coding region diversity was investigated by direct sequencing in 43 treatment-naive women in Rwanda.
- In addition, 10 isolates were analyzed for mutations 6 weeks after a single dose of nevirapine (PMTCT).
- Sequencing was done using Visible Genetics Truegene assay
- Phylogenetic analysis was performed using BLAST (NCBI), the neighbour joining method (Saitou) and bootstrap analysis (Felsenstein). A tree was drawn using Tree View programs.

Results (1)

- Phylogenetic analyses have shown 34 subtype A1, 6 subtype C and 2 subtype D strains from treatment naive patients.
- In addition, an A/C recombinant between the protease (PR) (subtype A1) and the reverse transcriptase (RT) (subtype C) was also identified.

subtypes

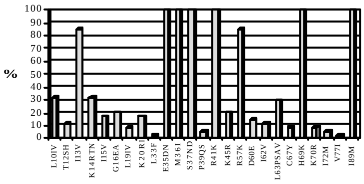




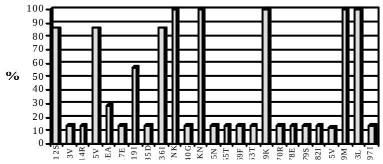
A/C (Bootstrap plot)

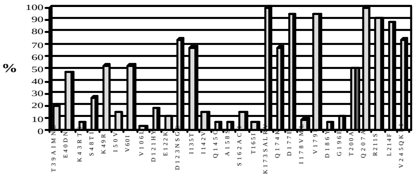
Results (2)

- In the PR coding region, high numbers of polymorphisms were found, including substitutions in secondary PR resistance sites.
- PR 35D, 36I and 37N were always present within subtype A as were PR 93L in subtype C strains.
- PR 10I/V, 20R, 33F, 77V were found in subtype A whereas PR 36I was highly prevalent in subtype C strains.

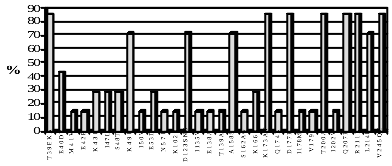


Protease, subtype A





Reverse transcriptase, subtype A



Reverse transcriptase, subtype C

Results (3)

- The A/C recombinant displayed substitutions related to resistance (PR 10, 33, 36 and RT 118).
- One key nevirapine resistance mutation (RT 181Y/C) was found in proviral DNA at six weeks

Conclusion

- Subtype C has emerged significantly in Rwanda on a background of subtype A.
- Substitutions similar to secondary protease inhibitor resistance mutations are common before treatment for each subtype whereas major resistance mutation may be archived after a single dose of nevirapine.
- Accordingly, the hypothesis of a genetic background effect in non-B strains has to be further addressed in programs of introduction of antivirals in Africa