



## Comparison of different tenofovir DF resistance algorithms

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**BACKGROUND :** Due to failures of current antiretroviral therapies, new anti-HIV drugs for salvage therapy are needed. Tenofovir disoproxil fumarate (TDF), a nucleotide reverse transcriptase (RT) inhibitor, has been recently approved. The list of RT amino acid substitutions - K65R, insertion 69, and TAMs (thymidine associated mutations) - which have been associated with reduced susceptibility to TDF is now better known but the interpretation of resistance differs between algorithms. We report here the prevalence of resistance strains in a clinical genotyping database using several algorithms.

**METHODS :** RT sequences were extracted from ABL database and submitted to the HIV ViroScorer© Large Scale release ([www.ablnetworks.org](http://www.ablnetworks.org)) for drug resistance determination. Six different algorithms were computed: ANRS (09/02), Detroit Medical Center (DMC) (06/02), Brazilian guidelines (GAV) (10/01), Rega (06/02), VGI Guidelines 6.0 (11/02) and Luxembourg (CHL) (01/03). Predicted levels of resistance range from sensitive (S), possible resistance (I) to resistance (R). We calculated the agreement between interpretations using the Light's Kappa (k) statistic.

**RESULTS :** Five-hundred high-quality RT sequences from 2002 were submitted. Resistance mutations were for RT: 184V/I(33%), 215Y/F(26%), 41L(23%), 67N(21%), 210W(14%), 70R(13%), 219Q/E(13%), 74V(9%), 151M(2%), 65R/Ins69(<1%). Specific mutation profiles were reported: 13% (M41L+L210W+T215Y/F), 9% (M41L+L210W+D67N), <1% (M41L+L210W+ at least one of: K219Q/E, K70R) and 9% (M41L+L210W+T215Y/F+D67N). Decreased susceptibility (I+R) for TDF was: 18% for ANRS, 15% (DMC), 1% (GAV), 24% (REGA), 26% (VGI) and 33% (CHL), respectively. Light's Kappa median (excluding GAV) was 0.74 [0.62-0.78] (inter-quartile range).

**CONCLUSIONS :** Except the GAV algorithm, decreased susceptibility of TDF ranged from 15% to 33% in samples from a clinical genotyping database. Agreement between algorithms was fairly good, but needs further improvement. Even if TDF is a nucleotide with a supposed lower level of cross-resistance to other NRTIs, the resistance mediated by TAMs acquired through prior exposure to NRTIs may limit the efficacy of this new drug.

## Abstracts