



Does HIV-1 subtype influence the results of drug resistance interpretation algorithms ?

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BACKGROUND : A preliminary study by Snoeck et al. (Abstract 40, 1st European HIV Drug Resistance Workshop 2003, Luxembourg) suggested on a small data set a possible influence of HIV subtype on concordance of interpretation algorithms. Largest disagreements were found for subtype J and D (PI only) viruses.

METHODS : In order to assess the influence of viral subtype in a large data set using appropriate statistics, we interpreted 2176 PRO and 2265 RT sequences respectively (N (PRO/RT) for subtype A=145/2002, B=1200/1200, C=318/312, D=131/188, F1=107/79, G=191/218, H=30/20, J=28/21, K=26/25) with five algorithms [ANRS(09/2002), DMC(01/2003), Brazil(10/2001), CHL4.4, Rega5.5], and computed Light's kappa statistics for 16 drugs in the different subtype groups. For each drug and subtype we calculated the kappa (K) value by algorithm pairs and then the median for all pairs. For statistical purposes, the intermediate answer class (i.e. possible resistance or I) was considered either as resistant (I=R) or in a second analysis as not resistant (I=S). Low K values for an I=R scenario point to disagreements in differentiating between sensitive and non-sensitive virus, low K values for an I=S scenario indicate non-concordance to differentiate between resistant and non-resistant virus.

RESULTS : Overall, there was no univocal trend showing that some subtypes constantly performed less well using these five interpretation algorithms. However, looking at results from both I=S and I=R analysis, subtypes D to K (especially H and K) yielded more frequently the poorest K scores for a given drug. At the same time, the highest K scores were also found, in other drug/subtype combinations, in this same cluster of subtypes D to K. Subtypes A to C gave generally less extreme K values. Subtype H showed large disagreements for all three NNRTI (Ks from 0.59-0.69), didanosine (K=0.29), abacavir (K=0.39), tenofovir (K=0.50), indinavir and amprenavir (Ks from 0.29 to 0.49). Subtype K had problems with didanosine and stavudine, but also with the PI amprenavir, indinavir and ritonavir (Ks from 0.19 to 0.51). Subtype J scored poorly (only in the I=R analysis) for stavudine and the four PI indinavir, nelfinavir, ritonavir and saquinavir (Ks from 0.08 to 0.55). Subtype D performed slightly less well for lamivudine in the I=R analysis (K=0.60), but not for PI as previously reported. Finally, bad K values (from 0.28 to 0.45) were found for F1 subtype (I=S only) for abacavir, lopinavir, nelfinavir and saquinavir.

CONCLUSIONS : Taken together our results show that a larger variability in genotypic drug resistance interpretations is found in subtypes D to K. Low K values for drug/subtype combinations may point to specific problems in algorithms which should be further investigated at a mutational level.

Abstracts