



Comparative Evaluation between Five Automated Resistance Interpretation Algorithms

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OBJECTIVE : To compare genotypic resistance interpretations provided by computerized algorithms.

METHODS : Five genotypic resistance interpretation algorithms (i.e. ANRS AC11, Data Analysis Plan (DAP), Detroit Medical Center, Federal University of Sao Paulo and Centre Hospitalier de Luxembourg) have been computerized for internet in the ViroScorer™ system (www.ablnetworks.com/online/online1.html). The program output is standardized and displays the drug resistance level for each drug and algorithm on the basis of a three-colour system. Agreement among resistance interpretations were calculated using the Light's Kappa : we calculated the Kappa (K) by algorithm pairs and then the median for the 10 pairs. The intermediate answer class (i.e. possible resistance) was considered either as "resistance" (I=R) or in a second analysis as "no resistance" (I=S). To interpret visually poor agreement, we plotted multiple correspondence analysis (mca) results.

RESULTS : 98 RT and 160 Pro sequences were submitted via internet. Most prevalent mutations in Pro were: L10I (23%), M36I (27%), M46I (13%), I54V (15%), L63P (70%), A71V (19%), V77I (40%), V82A (19%), and L90M (15%), and in RT: M41L (33%), K70R (16%), K103N (18%), M184V (46%), L210W (20%) and T215Y (32%). Kappa ranged from 0.20 to 0.95 (median 0.71 IQR 0.59-0.86) and from 0.30 to 0.89 (median 0.70 IQR 0.59-0.83), in the I=S and I=R analyses respectively. A good agreement ($K \geq 0.80$) between algorithms was found for efavirenz, nevirapine, delavirdine, and lamivudine in both analyses; for zidovudine and saquinavir in the I=R analysis; and for ritonavir and indinavir in the I=S analysis. Abacavir, amprenavir and nelfinavir only showed a moderate level of agreement, while a poor agreement ($K < 0.60$) was observed for stavudine, didanosine and zalcitabine. The mca graphs indicated that only the DAP interpretation is discordant for stavudine and outlined an important variability for didanosine and zalcitabine, even if some algorithm pairs were concordant.

CONCLUSIONS : For most drugs a similar resistance interpretation was obtained with different algorithms. Algorithms largely diverge in the interpretation of resistance to stavudine, didanosine and zalcitabine. Further work is required to determine a more comprehensive way for resistance interpretation of these drugs, and to understand the relation between interpretation and clinical outcome.

Abstracts