Comparison of HIV-1 Protease Inhibitor Susceptibility Results in Viremic Protease Inhibitor(PI)-Experienced Patient Samples Analyzed by Phenotyping and by Five Resistance Algorithms

Abstracts

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OBJECTIVE: Phenotypic HIV-1 drug resistance testing has been demonstrated to aid in therapy management for antiretroviral-experienced patients. Genotypic analyses can be done more rapidly and economically, and the use of algorithms utilizing genotypic data to predict drug resistance is becoming more common. Agreement between the actual phenotype and the predicted result may be impacted for newly approved drugs for which few phenotypic assays are available. We assessed the agreement between the actual phenotypic results and those predicted by five predictive algorithms for the marketed PIs.

METHODS: Subjects received 1 to 4 concurrent or consecutive non-boosted PI-containing regimens, including indinavir, saquinavir, nelfinavir, ritonavir or amprenavir for >4 months. HIV isolated from plasma from virologically-rebounding or non-responding subjects (N=207) was analyzed for phenotypic drug susceptibility by VIRCO Antivirogram, and HIV-1 mutations were detected using the ABI HIV Genotyping System. Genotypic data was analyzed using the ABL HIV ViroScorer™, which provides individual predictive algorithm results based upon the following algorithms: ANRS AC11; Detroit Medical Center, USA; Grupo Aconselhamento Virologico (GAV), Brazil; CHLv3.2, Luxembourg; and Rega v5.0, Belgium. Kappa scores were used to compare agreement of the phenotype and predictive algorithms.

RESULTS : Using the VIRCO fold-resistance (FR) cut-offs to determine susceptibility, 60%, 35%, 63%, 71%, 66% and 57% of the samples had decreased susceptibility to lopinavir (=2.5), amprenavir (=2.5), indinavir (=3), nelfinavir (=4), ritonavir (=3.5) or saquinavir (=2.5). Using a =10FR cut-off, 28% of the samples had decreased lopinavir susceptibility. For the five algorithms, the kappa score ranged as follows lopinavir (FR=2.5) 0.271-0.683, lopinavir (FR=10) 0.321-0.369, amprenavir 0.273-0.563, indinavir 0.461-0.583, nelfinavir 0.517-0.665, ritonavir 0.542-0.780 and saquinavir 0.449-0.670, with moderate or greater concordance (=0.4 kappa) observed in all algorithms for the latter four drugs. The largest range in kappa was seen for lopinavir when compared at the >2.5FR cut-off. Comparison using the =10FR cut-off reduced the range but also decreased the overall agreement of the data. The overall kappa scores for the assays using the lopinavir (FR=2.5) were: 0.626, 0.558, 0.557, 0.518, and 0.461, for ANRS AC11; Detroit; GAV; CHLv3.2; and Rega v5.0, respectively. There was little difference in the overall kappas using lopinavir FR=10.

CONCLUSIONS : The predictive algorithms overall had moderate agreement with the actual phenotypic results for the protease inhibitors as a class. The widest variation in predictability was seen for lopinavir, with the concomitant reduction in data concordance if the phenotypic cut-off was raised. This suggests there are additional mutations or weighting factors that impact response to lopinavir that need to be included in future versions of the algorithms.