ABSTRACT 167

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Drug resistance among therapy-naive HIV-infected patients studied by sequencing and VERSANT™ HIV-1 resistance assays (LiPA) has limited impact on treatment response.

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AIM: To study baseline drug-resistance among therapy-naive HIV-infected patients diagnosed in 2000 in Belgium, and to assess its impact on treatment response.

METHODS: Retrospective samples from therapy-naive patients diagnosed in 2000 were collected through the Belgian AIDS Reference Laboratories. Only baseline samples with a viral load >1000 c/ml from patients who subsequently started and remained on unchanged antiviral therapy for at least 3 months were included. Sequencing (ViroSeq V2 or in-house) and VERSANT™ HIV-1 Resistance Assay (LiPA) (available for research use only through Bayer Corporation) of the reverse transcriptase (RT) and protease (PRO) gene were performed retrospectively. Using the BLAST algorithm, sequences were identified as either belonging to subtype B or not. Resistance-associated mutations were identified and interpreted according to the REGA v5.0 rule-based algorithm. Values of 1, 0.5 or 0 were attributed to drugs in the prescribed regimen that scored as susceptible, reduced susceptible or resistant respectively, and summed in a Susceptibility Score (SS) based on sequence data only (S_SS), and on the combined sequence and LiPA data (SL_SS). CD4 count, log Viral Load (log VL) and treatment changes were monitored 3, 6 and 12 months after the start of treatment.

RESULTS: Ninety-three samples were collected from four participating centers. Reverse transcriptase and PRO were successfully sequenced in 80 (86%) and 83 (89%) of the samples, respectively. LiPA was successful in 96.7% for RT, 94.6% for protease 30-84, and 93.5% for protease 90. Non-B subtype was predominant (71%). Based on sequencing, 4 (5%), 6 (7.5%) and 41 (49%) of viruses were scored reduced susceptible or resistant to at least one nucleoside reverse transcriptase inhibitor (NRTI), non-nucleoside reverse transcriptase inhibitor (NNRTI) or protease inhibitor (PI), respectively. For PI, this was entirely based on the presence of secondary mutations. The mean S_SS was 2.97, which was significantly higher than the mean SL_SS of 2.88 (P=0.003). No significant correlation was found between S_SS or SL_SS and log VL drop at 3 months. Of the patients with one year follow-up and complete sequencing data, 16% (12/74) had virological therapy failure (non-responders, NR). No significant difference in S_SS, SL_SS, CD4 count or log VL was demonstrated between responders (R) and NR. Mean SL_SS was not significantly higher in R than in NR (2.91 vs 2.66). Only treatment with NRTIs for which the virus was scored resistant or reduced susceptible was significantly associated with treatment failure (OR: 0.08; 0.0068–0.9905).

CONCLUSIONS: In Belgium in 2000, the prevalence of treatment-naive HIV-infected patients with resistance-associated mutations was found to be substantial, with resistance or reduced susceptibility to at least one drug in almost half the patients. Although baseline susceptibility score did not predict therapy response, a significant but weak association was found between treatment failure and treatment with NRTIs for which the virus was scored resistant or reduced susceptible.