Introduction

• HIV-1 genotypic drug resistance (DR) testing requires availability of up-to-date interpretive algorithms and software applications designed for use in clinical laboratories.
• Several HIV-1 genotypic DR interpretive applications, based on either genotypic sequencing (ViroSeq-HIV and ABL DPM) or NGS methods (DeepChek-HIV), are currently available from ABL (Advanced Biological Laboratories, Inc.) to generate interpretive reports intended for clinical use (Fig. 1).
• This study was performed to assess reporting differences between the ViroSeq HIV-1 Genotyping System, version 2.0 (Abbott Molecular, Inc.) and an FDA-registered ABL DPM software application using specimens obtained from treatment-experienced, HIV-1 infected patients.

Materials and Methods

• Thirty (30) clinical plasma specimens belonging to a cohort of treatment-experienced, HIV-1 infected patients were tested with the FDA-approved ViroSeq HIV-1 Genotyping System, version 2.0 and ViroSeq HIV-1 Genotyping System Software, version 3.8 (VQ; Abbott Molecular, Inc.).
• HIV-1 sequences were further analyzed with an FDA-registered ABL (Advanced Biological Laboratories, Inc.) data processing module (DPM) software application, which can be used for genotypic HIV-1 DR interpretation (ABL DPM HIVdb; HIVdb) based on the Stanford HIVdb Program (http://www2.stanford.edu/group/hivdb/group) and for predictive phenotypic resistance interpretation (ABL DPM Geno2Pheno; G2P) based on Geno2Pheno 3.3 (http://virology.anl.org) (Fig. 2).
• HIV-1 DR interpretation results from VQ, HIVdb, and G2P were analyzed (Fig. 3).

Results

• A total of 570 individual drug resistance interpretations were generated from the 30 sequences.
• On an average, HIVdb showed resistant (R) results (27.2%) more frequently than VQ (25.8%). VQ was more likely (64.4%) to show susceptible (S) results than HIVdb (53.9%) and G2P (56%) (Fig. 4).
• Compared to VQ results as the reference, HIVdb yielded 73.3% “positive” minor discordance (S vs. Intermediate or I vs. R), 10% “negative” minor discordance (I vs. S, or R vs. I), and no “major” major discordance (S vs. R) (Fig. 5).
• Among specimens producing the same interpretation results with HIVdb and G2P, 50% yielded different results by VQ. 50% “positive” minor discordance (S vs. I, or I vs. R), 6.7% “negative” minor discordance (I vs. S, or R vs. I), 3.3% of “positive” major discordance (S vs. R), and no “negative” major discordance (R vs. S) (Fig. 5).
• At the drug level, differences were observed as shown in Fig. 6.

Conclusions

• Different interpretations of HIV-1 DR were observed among the interpretative software applications and databases evaluated in this study.
• Access to continually updated databases may improve reliability of HIV-1 DR interpretations for optimal antiretroviral therapy.

Comparison of interpretive applications used for HIV-1 drug resistance determination

Dimitri Gonzalez1, Carl Bommersbach2, Olga Fernando3, Jeffrey Germer1, Matthieu Barralon2, Ronan Bouline3, Chalom Sayada3, Joseph Yao2
1 ABL Therapeutics, Spain SL, Barcelona, Spain.
2 Mayo Clinic, Rochester, MN, U.S.A.
3 ABL SA, Luxembourg.

Fig. 1: Examples of HIV-1 genotypic DR reports for ViroSeq-HIV (CE-IVD) (A & B), ABL DPM (FDA-reg) (C), and DeepChek-HIV (CE-IVD) (D).

Fig. 2: Data analysis workflow for ABL software systems.

Fig. 3: Study overview.

Fig. 4: Drug resistance interpretations for VQ, HIVdb and G2P.

Fig. 5: Percentages of sequences with different drug resistance interpretations.

Fig. 6: Repartition per drug of results with a different interpretation (A) or a one-level increase (B) for VQ among sequences producing the same interpretation results with HIVdb and G2P.