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

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Introduction

- HIV-1 genotypic drug resistance (DR) testing requires availability of up-to-date interpretative algorithms and software applications designed for use in clinical laboratories.
- Several HIV-1 genotypic DR interpretive applications, based on either Sanger sequencing (ViroScore-HIV and ABL DPM) or NGS methods (DeepChek-HIV), are currently available from ABL (Advanced Biological Laboratories S.A.) 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.

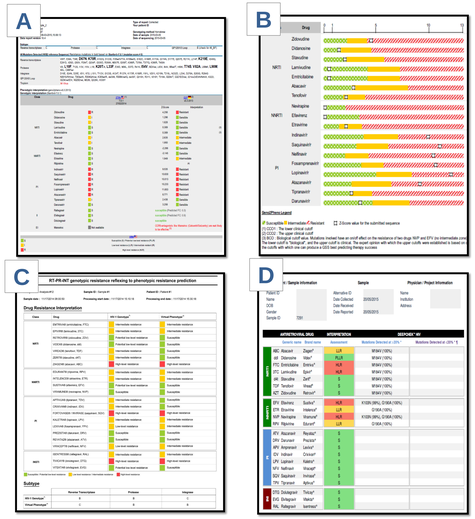

Fig. 1: Examples of HIV-1 genotypic DR reports for ViroScore-HIV (CE-IVD) [A & B], ABL DPM (FDA-reg) [C], and DeepChek-HIV (CE-IVD) [D].

Materials and Methods

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

- 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 3.0.1 (VQ; Abbott Molecular, Inc.).
- HIV-1 sequences were further analyzed with an FDA-registered ABL (Advanced Biological Laboratories S.A.) 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://sierra2.stanford.edu/sierra/servlet/JSierra) and for predictive phenotypic resistance interpretation (ABL DPM Geno2Pheno; G2P) based on Geno2Pheno 3.3 (http://www.geno2pheno.org) (*Fig. 2*).
- HIV-1 DR interpretation results from VQ, HIVdb and G2P were analyzed (*Fig. 3*).

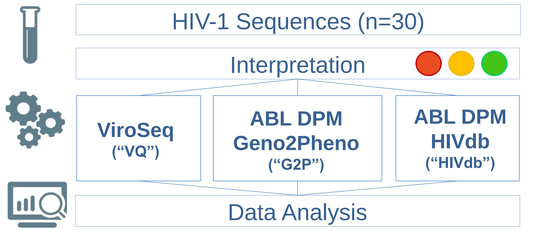

Fig. 3: Study overview.

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 (53.7%) and G2P (56%) (*Fig. 4*).

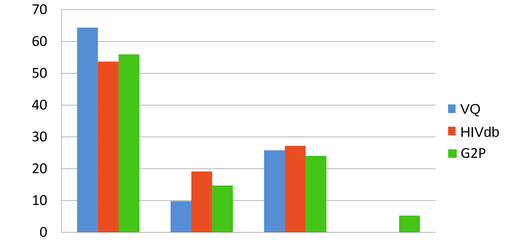

Fig. 4: Drug resistance interpretations for VQ, HIVdb and G2P.

- Compared to VQ results as the reference, HIVdb yielded 73.3% "positive" minor discordance (S vs. Intermediate or I, or I vs. R), 10% 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*).
- 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*.

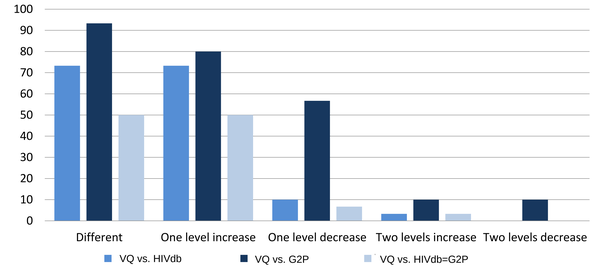

Fig. 5: Percentages of sequences with different drug resistance interpretations.

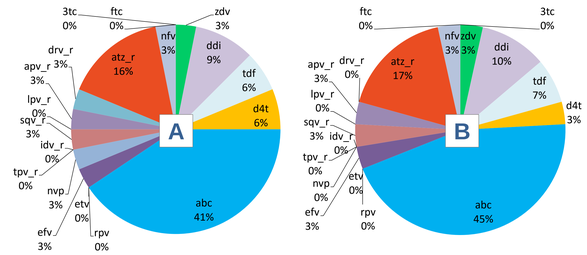

Fig. 6: Repartition per drug of results with a different interpretation (A) or a one-level increase (B) for VQ among sequences producing the same interpretation results with HIVdb and G2P.

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 reliably of HIV-1 DR interpretations for optimal antiretroviral therapy.