Validation of New Informatics Systems for Routine HIV-1 Genotypic and Virtual Phenotypic Antiviral Drug Resistance Analyses in Clinical Laboratories

Dimitri Gonzalez1, Benjamin Digmann2, Matthieu Barralon3, Ronan Bouline3, Chalom Sayada2, Joseph Yao2

1 ABL Therapeutic SpA-St. Barcelona, Spain
2 Therapeutic with \textit{v}1.0; Advanced Biological Laboratories S.A., Luxembourg
3 ABL SA, Luxembourg.

Background

- Clinical laboratories performing testing for detection and analyses of HIV-1 genotypic drug resistance need reliable and up-to-date software and database solutions to optimally analyze Sanger sequencing-generated data for interpretative reporting of results.

Methods

- Through a retrospective analysis of HIV-1 reverse transcriptase (RT) and protease (PR) sequences generated from the Trugene HIV-1 Genotyping assay (TFG, Siemens Healthcare Diagnostics Inc., Tarrytown, NY), for 100 selected unique clinical plasma specimens obtained from HIV-1-infected patients, we evaluated 2 analytical informatics systems (Fig. 1).
  - A newly FDA-registered data processing module software application (DPM v1.0, Advanced Biological Laboratories S.A., Luxembourg) based on several external drug resistance (DR) databases, including Stanford HIVdb (SD) and Geno2Pheno (G2P).
  - A research-use-only ViroScore (VS) software application.

- Results of drug resistance to NRTI, NNRTI and PI were compared with the Guidelines version 17 interpretation generated from Trugene HIVdb® (B), ViroScore (A), and Geno2Pheno (C).

- Through a retrospective analysis of HIV-1 reverse transcriptase (RT) and protease (PR) sequences generated from the Trugene HIV-1 Genotyping assay (TFG, Siemens Healthcare Diagnostics Inc., Tarrytown, NY), for 100 selected unique clinical plasma specimens obtained from HIV-1-infected patients, we evaluated 2 analytical informatics systems (Fig. 1).
  - A newly FDA-registered data processing module software application (DPM v1.0, Advanced Biological Laboratories S.A., Luxembourg) based on several external drug resistance (DR) databases, including Stanford HIVdb (SD) and Geno2Pheno (G2P).
  - A research-use-only ViroScore (VS) software application.

- Results of drug resistance to NRTI, NNRTI and PI were compared with the Guidelines version 17 interpretation generated from Trugene HIVdb® (B), ViroScore (A), and Geno2Pheno (C).

Validation of New Informatics Systems for Routine HIV-1 Genotypic and Virtual Phenotypic Antiviral Drug Resistance Analyses in Clinical Laboratories

Dimitri Gonzalez1, Benjamin Digmann2, Matthieu Barralon3, Ronan Bouline3, Chalom Sayada2, Joseph Yao2

1 ABL Therapeutic SpA-St. Barcelona, Spain
2 Therapeutic with \textit{v}1.0; Advanced Biological Laboratories S.A., Luxembourg
3 ABL SA, Luxembourg.

Background

- Clinical laboratories performing testing for detection and analyses of HIV-1 genotypic drug resistance need reliable and up-to-date software and database solutions to optimally analyze Sanger sequencing-generated data for interpretative reporting of results.

Methods

- Through a retrospective analysis of HIV-1 reverse transcriptase (RT) and protease (PR) sequences generated from the Trugene HIV-1 Genotyping assay (TFG, Siemens Healthcare Diagnostics Inc., Tarrytown, NY), for 100 selected unique clinical plasma specimens obtained from HIV-1-infected patients, we evaluated 2 analytical informatics systems (Fig. 1).
  - A newly FDA-registered data processing module software application (DPM v1.0, Advanced Biological Laboratories S.A., Luxembourg) based on several external drug resistance (DR) databases, including Stanford HIVdb (SD) and Geno2Pheno (G2P).
  - A research-use-only ViroScore (VS) software application.

- Results of drug resistance to NRTI, NNRTI and PI were compared with the Guidelines version 17 interpretation generated from Trugene HIVdb® (B), ViroScore (A), and Geno2Pheno (C).

- Through a retrospective analysis of HIV-1 reverse transcriptase (RT) and protease (PR) sequences generated from the Trugene HIV-1 Genotyping assay (TFG, Siemens Healthcare Diagnostics Inc., Tarrytown, NY), for 100 selected unique clinical plasma specimens obtained from HIV-1-infected patients, we evaluated 2 analytical informatics systems (Fig. 1).
  - A newly FDA-registered data processing module software application (DPM v1.0, Advanced Biological Laboratories S.A., Luxembourg) based on several external drug resistance (DR) databases, including Stanford HIVdb (SD) and Geno2Pheno (G2P).
  - A research-use-only ViroScore (VS) software application.

- Results of drug resistance to NRTI, NNRTI and PI were compared with the Guidelines version 17 interpretation generated from Trugene HIVdb® (B), ViroScore (A), and Geno2Pheno (C).

Results

- Among 100 selected TG sequences generated at the Mayo Clinic laboratory from March 2013 through May 2014, agreement of DR interpretative results between DPM v1.0 and VS was >99.9%.
- Agreement between TG and SD and between TG and G2P were both only 17%.
- Median % agreement in DR interpretation between TG and SD, TG and G2P, SD and G2P are showed in Table 1.
- Detailed % agreement for each drug or drug combination are shown in Table 2.
- With TG as the reference result, SD and G2P generated:
  - “Positive” minor discordance, defined as susceptible S vs. intermediate I, or I vs. resistant R to ≥1 drug, in 66% and 56% of results, respectively.
  - “Negative” minor discordance, defined as susceptible S vs. intermediate I, or I vs. resistant R to ≥1 drug, in 66% and 56% of results, respectively.
  - Major discordance (S vs. R) in 6% and 15%.
  - And major discordance (R vs. S) in 1% and 19% of subjects, respectively.

Conclusions

- DPM v1.0 and VS were reliable to analyze RT and PR sequences in HIV-1 drug resistance testing for both research and routine clinical use.
- Differences in interpretation of drug resistance observed were most likely due to differences in the interpretive guidelines used by these databases.