

Software Dependent Differences in HIV-1 Drug **Resistance Determination.**





October 14 – 16, 2015

Introduction

Dimitri Gonzalez¹, Ronan Boulmé¹, Chalom Sayada¹, Ah-Young Sung², Boyka Baltadjieva², Michael Michalov², Lech Mazur²

¹ ABL SA, Luxembourg. ² ACL Central Laboratory Rosemont, IL USA.

<u>Tab. 1</u>: Evaluated HIV-1 drug resistance interpretation software systems.

• Software for HIV-1 genotypic drug resistance testing is routinely used to generate clinical drug resistance interpretations. In this study we compare the differences found in the results obtained with 3 distinct software (Tab. 1).

Software	Supplier	Registration		Guidelines
ViroSeq Genotyping Software	Abbott	FDA-approved	•	ViroSeq v3.0.0.32 (VS)
DPM v1.0 (Research use only, RUO)	ABL SA	FDA-registered	•	Genotypic-based: HIVdb v7.0.1 (SD) Others (>7 algorithms) Virtual-Phenotypic-based: Geno2pheno v3.3 (G2P)
ViroScore-HIV® v3.20 (RUO)	ABL SA	CE-IVD / RUO	•	Same as DPM v1.0

Methods

• HIV sequencing data of forty five (45) clinical samples belonging to treatment-experienced patients were analyzed using ViroSeq (VS) Genotyping Software v3.0.0.32.

- All (VS) results were compared to the FDAregistered DPM product and to the RUO ViroScore-HIV® system; both products from Advanced Biological Laboratories
- ViroScore® include several knowledge databases i.e. Stanford HIVdb v7.0.1 (SD) or the virtualphenotypic-based algorithm from Geno2Pheno ∨3.3 (G2P) – Fig. 1.



Fig. 1: Samples analysis methodology overview.

	ance Interpretati	on		2762		100	
Class	Drug		HIV	/-1 Genotype [™]	Virt	ual Phenotype ⁽²⁾	
	EMTRIVA® (emtricitat	ine, FTC)		Intermediate resistance		Intermediate resistance	
	RETROVIR® (zidovud	RETROVIR® (zidovudine, ZDV)		Potential low-level resistance		Susceptible	
NRTI	VIDEX® (didanosine,	VIDEX® (didanosine, ddl)		Potential low-level resistance		Susceptible	
	VIREAD® (tenofovir, 1	VIREAD® (tenofovir, TDF)		Intermediate resistance		Susceptible	
	ZERIT® (stavudine, de	ZERIT® (stavudine, d4T) ZIAGEN® (abacavir, ABC)		Intermediate resistance		Susceptible	
	EDURANT® (rilpivirine	EDURANT® (rilpivirine, RPV)		Intermediate resistance		Intermediate resistance	
NNRTI	INTELENCE® (etravir	INTELENCE® (etravirine, ETR)		Intermediate resistance		Intermediate resistance	
	SUSTIVA® (efavirenz, EFV)			Potential low-level resistance		Susceptible	
	VIRAMUNE® (nevirapine, NVP)			Susceptible		Susceptible	
	APTIVUX® (tipranavir, TDV)			Intermediate resistance		Susceptible	
	CRIXIVAN® (indinavir, IDV)			Intermediate resistance		Susceptible High-level resistance	
РІ	KALETRA® (lopinavir, LPV)			Intermediate resistance		Intermediate resistance	
	LEXIVA® (fosamprena	LEXIVA® (fosamprenavir, FPV)		Low-level resistance		Intermediate resistance	
	PREZISTA® (darunav	r, DRV)		Susceptible		Susceptible	
	REYATAZ® (atazanav	REYATAZ® (atazanavir, ATV)		Susceptible		Susceptible	
	VIRACEPT® (nelfinav	r, NFV)		Low-level resistance		intermediate resistance	
INSTI	ISENTRESS® (raitegr TIVICAY® (doluteoray	ISENTRESS® (raltegravir, RAL)		Intermediate resistance		Intermediate resistance	
	VITEKTA® (elvitegravir, EVG)			Potential low-level resistance		Susceptible	
Reverse Transcriptase HIV-1 Genotype ^{re} B		Transcriptase B		Protease B		Integrase C	
Virtual Phenotype	0	С		В		В	_
Class	Drug	0 1		5		10	
Class	Drug Zidovudine			اً بلار	//	10	//
Class	Drug Zidovudine Didanosine			5 /¤///////////////////////////////////		10	
Class	Drug Zidovudine Didanosine Stavudine			5 /¤///////////////////////////////////			
Class	Drug Zidovudine Didanosine Stavudine Lamivudine		00	5 /Ц///////////////////////////////////			
Class	Drug Zidovudine Didanosine Stavudine Lamivudine Emtricitabine		00				
Class	Drug Zidovudine Didanosine Stavudine Lamivudine Emtricitabine Abacavir		00				
Class	Drug Zidovudine Didanosine Stavudine Lamivudine Emtricitabine Abacavir Tenofovir		00 00				
Class	Drug Zidovudine Didanosine Stavudine Lamivudine Emtricitabine Abacavir Tenofovir		00 00				
Class	Drug Zidovudine Didanosine Stavudine Lamivudine Emtricitabine Abacavir Tenofovir Nevirapine		00 00				
Class NRTI	Drug Zidovudine Didanosine Stavudine Lamivudine Emtricitabine Abacavir Tenofovir Nevirapine Efavirenz	0 1 000000000 00000000 00000000 00000000	00 00				
Class NRTI	Drug Zidovudine Didanosine Stavudine Lamivudine Emtricitabine Abacavir Tenofovir Nevirapine Efavirenz Etravirine	0 000000000000000000000000000000000000	00 00 0				
Class NRTI NNRTI	Drug Zidovudine Didanosine Stavudine Lamivudine Emtricitabine Abacavir Tenofovir Nevirapine Efavirenz Etravirine Indinavir/r	0 1 000000000 00000000 00000000 00000000					
Class NRTI	Drug Zidovudine Didanosine Stavudine Lamivudine Emtricitabine Abacavir Tenofovir Nevirapine Efavirenz Etravirine Indinavir/r Saquinavir/r	0 000000000 00000000 00000000 00000000					
Class NRTI	Drug Zidovudine Didanosine Stavudine Lamivudine Emtricitabine Abacavir Tenofovir Nevirapine Efavirenz Etravirine Indinavir/r Saquinavir/r	0 1 000000000 00000000 00000000 00000000					
Class NRTI	Drug Zidovudine Didanosine Stavudine Lamivudine Emtricitabine Abacavir Tenofovir Nevirapine Efavirenz Etravirine Indinavir/r Saquinavir/r Nelfinavir	0 1 000000000 00000000 00000000 00000000					
Class NRTI NNRTI	Drug Zidovudine Didanosine Stavudine Lamivudine Emtricitabine Abacavir Tenofovir Tenofovir Nevirapine Efavirenz Etravirine Indinavir/r Saquinavir/r Nelfinavir Fosamprenavir/r	0 000000000 00000000 00000000 00000000					
Class NRTI NNRTI	Drug Zidovudine Didanosine Stavudine Lamivudine Emtricitabine Abacavir Tenofovir Nevirapine Efavirenz Etravirine Indinavir/r Saquinavir/r Nelfinavir Fosamprenavir/r	0 1 000000000 00000000 00000000 00000000					
Class NRTI NNRTI	Drug Zidovudine Didanosine Stavudine Lamivudine Emtricitabine Abacavir Tenofovir Nevirapine Efavirenz Etravirine Indinavir/r Saquinavir/r Nelfinavir Fosamprenavir/r Lopinavir/r	0 000000000 00000000 00000000 00000000					
Class NRTI NNRTI PI	Drug Zidovudine Didanosine Stavudine Lamivudine Erntricitabine Abacavir Tenofovir Tenofovir Nevirapine Efavirenz Etravirine Indinavir/r Saquinavir/r Nelfinavir Fosamprenavir/r Lopinavir/r Atazanavir/r	0 000000000 00000000 00000000 00000000					
Class NRTI NNRTI	Drug Zidovudine Didanosine Stavudine Lamivudine Emtricitabine Abacavir Tenofovir Nevirapine Efavirenz Efavirenz Indinavir/r Saquinavir/r Saquinavir/r Saquinavir/r Lopinavir/r Lopinavir/r Atazanavir/r Darunavir/r	0 000000000 00000000 00000000 00000000					

Results

- Overall, G2P was the algorithm showing fewer interpretations classified as "Resistant" (8.9%, compared to 9.4% with SD and 9.2% with VS) and VS was the one showing the highest percentage of "Susceptible" interpretations (86.1%, compared to 75.3% with SD and 78.3% with G2P) – Fig. 2.
- For 41 of the samples we retrieved resistance interpretations for 19 drugs with all three algorithms, allowing us to compare 779 drug resistance results between algorithms. In 34.1% of the samples, VS reported different resistance interpretations for at least one drug when compared to SD, with a 1-level lower resistance value (from Resistant [R] to Intermediate [I] or from I to Susceptible [S]).
- When considering only the interpretations where SD was in agreement with G2P (714), VS reported



1-level lower resistance values for at least one drug in 12.2% of the samples – Fig. 3.

• At the drug level, differences were observed as shown in Fig. 4.

> Fig. 4: Repartition per drug of results showing a different interpretation (A) or a one-level increase (B) for VS among specimens showing same interpretation results between SD and G2P.

Conclusions

• Laboratories performing DR testing should be aware of alternative interpretive systems which could be used to supplement their existing DR reports.



http://diag.ablsa.com

contact@ablsa.com

