Evaluation of a commercial assay whole genome HIV-1 using next-generation sequencing for the detection of HIV-1 drug resistance mutations

O. Ardizzoni[1] , L. Naldi[1], J. Bernard[1], L. Deblir[2], D. Gonzalez[1], R. Boulme[1], C. Sayada[2], S. Mohamed[1].

[1]ABL FRANCE - Marseille (France), [2]ABL LUXEMBOURG - Luxembourg (Luxembourg)

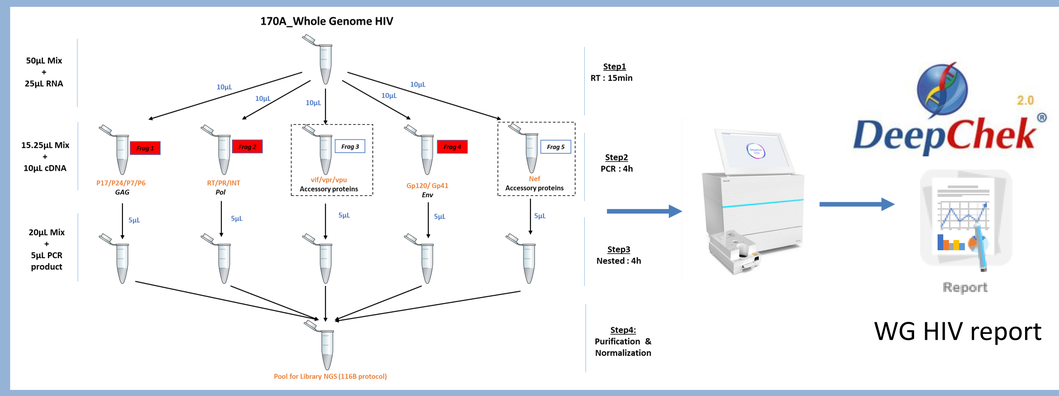
32nd ECCMID Lisbon, Portugal 23–26 April 2022

Background

Drug-resistance mutations are routinely detected using standard Sanger sequencing, which does not detect minor variants with a frequency below 15%. NGS is thus becoming the new standard for genotypic drug resistance testing for HIV. The global spread of SARS-CoV-2 mobilized both the public and private sector and resulted in a rapid development of solutions focused on SARS-CoV-2 detection and sequencing. Many laboratories are now equipped to perform Whole Genome Sequencing (WGS). The objective of this study was to evaluate the performance of the WGS of HIV-1 assay.

Methods

A total of 10 positive samples were prepared, extracted (Roche MagNa Pure 24, Roche). Three HIV-1 genomic targets were amplified using the CEIVD DeepChek® Assays PR/RTand INT regions (ABL) and were sequenced using the SANGER SeqStudio system (Applied Biosystem). The whole genome HIV-1 was amplified using the DeepChek® Assays Whole Genome HIV-1 (ABL) and was sequenced using the NGS iSeq100 (Illumina). Sequences were compared to those obtained by Sanger Sequencing. HIV-1 QCMD and AcroMetrix™ HIV Mutant (Thermofisher scientific) were sequenced. DeepChek® HIV-1 Whole Genome software (ABL) was used for the interpretation of drug resistance.



Results

The median coverage per sample for the WGS of HIV-1 was 17’500 reads. High analytical reproducibility and repeatability were evidenced by Percent Agreement being 100%. Duplicated samples in two different NGS runs were 100% homologous. NGS detected all the mutations found by Sanger sequencing and identified additional resistance variants. The score of the QCMD panel detection of drug resistance mutations for RT/PR and INT were 339/339 and 125/125, respectively. All AcroMetrix™, Seraseq mutations were detected using WG HIV kit

Sample	Ref	Viral Load	subtype	RT mutations of interest	PR mutations of interest	INT mutations of interest
1	HIV Zeptometrix	2.10^7 TCID50	B	wildtype	wildtype	wildtype
2	HIV Zeptometrix	2.10^5 TCID50	B	wildtype	wildtype	wildtype
3	HIV Zeptometrix	2.10^1 TCID50	B	wildtype	wildtype	wildtype
4	HIV Acrometrix	140,000 cp/mL	B	M41L, T69D, K70R, Y181C, T215Y	L10R, D30N, A71V, L90M	No mutation
5	HIV Acrometrix	28,000 cp/mL	B	M41L, T69D, K70R, Y181C, T215Y	L10R, D30N, A71V, L90M	No mutation
6	HIV Acrometrix	20,000 cp/mL	B	M41L, T69D, K70R, Y181C, T215Y	L10R, D30N, A71V, L90M	No mutation
7	HIV Seraseq	20,000cp/mL	B	L10I	T215Y, K219Q	No mutation
8	QCMD1	4.57 Log10 cp/mL	C	M41L, E44D, D67N, T69D, A98G, M184V, L210W, T215Y	L10F, D30N, N88D	No mutation
9	QCMD2	4.24 Log10 cp/mL	A/G	No mutation	No mutation	No mutation
10	QCMD3	5.16 Log10 cp/mL	B	No mutation	K43T (19,63%), M46I, I54V, V82A, L90M	No mutation

Conclusions

This study is the first evaluation of the DeepChek® Assays Whole Genome HIV-1 (ABL) using the iSeq100 system combined with an easy software. The NGS should occupy a major place in HIV resistance surveillance and clinical care, thanks to its decreasing costs (due to COVID-19 pandemic) and ability to reveal resistant variants and study their impact; especially on the new capsid/maturation inhibitors and detection of potential new clinically relevant mutations in the HIV genome.

References

1. Mohamed S, Penaranda G, Gonzalez D, Camus C, Khiri H, Boulme R, et al. Comparison of ultra-deep versus Sanger sequencing detection of minority mutations on the HIV-1 drug resistance interpretations after virological failure. AIDS 2014,28:1315-1324.
2. Mohamed S, Ravet S, Camus C, Khiri H, Olive D, Halfon P. Clinical and analytical relevance of NNRTIs minority mutations on viral failure in HIV-1 infected patients. J Med Virol 2013; 86:394–403.

Contact information

Sofiane Mohamed, PhD:
s.mohamed@ablsa.com

https://www.ablsa.com/