Viral load measurement in HIV-1 samples with highly mutated Integrases

PP-157

Robert Ehret, Emre Ahmed, Stefan Breuer, Martin Obermeier

Medical Center for Infectious Diseases, Berlin (MIB)

Contact: Ehret@mvz-mib.de

BACKGROUND

Most HIV guidelines include first-line treatment combinations with integrase inhibitors. Although highly conserved, this increasing use exerts selection pressure on the integrase genes so that resistance-associated mutations are selected. Some qPCR assays use integrase as one of the targets for their probe-based measurements. In this study, we focus on the measurement of HIV-1 viral load in viruses with highly mutated integrases.

RESULTS

The samples distributed across 9 different subtypes (A, A1, A6, B, C, D, F, CRF01_AE, CRF02_AG) showed between 9 and 31 deviations in the approximately 300 amino acids of the integrase compared to the consensus B wild type. In these amino acid changes up to five different resistance associated mutations in one sample were detected. Overall the mutations let to 7 samples with resistance against at least one integrase inhibitor and to restrictions to integrase inhibitor use for 21 samples. The correlation of the HIV-1 viral load results from both tests was high and achieved an R^2 of 0.9484. No false quantifications were detected within the viral load range of 2.8 to 6.2 log IU/mL.

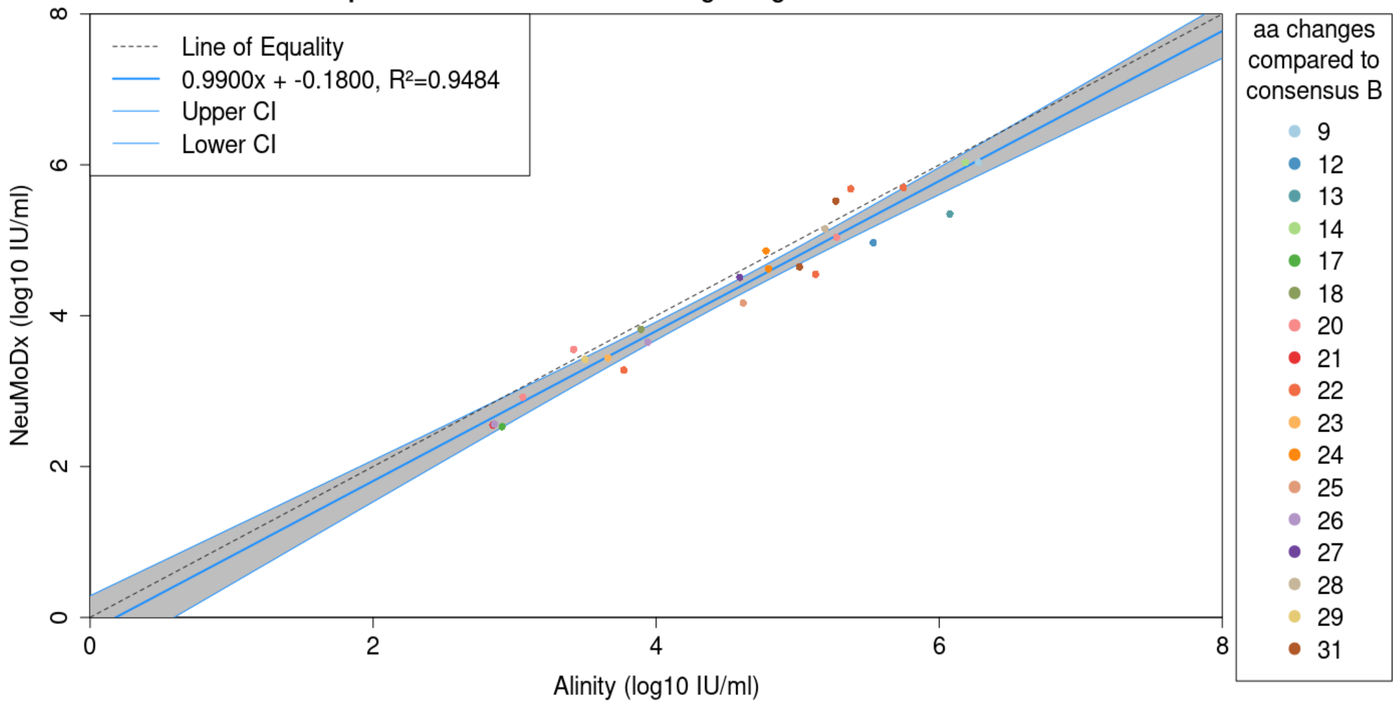

Fig. 1: Deming regression of samples with known aminoacid differences to HIV-1 consensus B in the Integrase gene, log IU/mL Alinity m vs. NeuMoDx

METHODS

As part of a larger comparative study with 500 samples studying the performance of the NeuMoDx HIV-1 Quant assay (QIAGEN) with the more established Alinity m HIV-1 assay (Abbott), we analysed 25 samples of different HIV-1 subtypes with highly mutated integrase genes. The routine samples were sequenced for resistance testing and stored at -20°C. After thawing they were tested in parallel with both systems in order to document a possible bias due to non-matching primers/probes in the integrase gene target regions of both assays.

CONCLUSIONS

A high correlation between the two assays was demonstrated with a specific focus on highly mutated integrase genes. Even with amino acid substitutions of more than, no incorrect quantifications were observed. The true random access capability of the NeuMoDx platform is a valuable tool for clinical routine HIV-1 viral load measurement and performance was not impacted by the highly-mutated samples tested in this study.

Tab. 1: 25 highly mutated Integrasegenes of different HIV-1 subtypes with drug resistance interpretation by HIV-GRADE

sample No.	HIV subtype	aminoacid changes	Integrase resistance mutations	HIV-1 viral load [log IU/ml]	Bictegravir	Cabotegravir	Dolutegravir bid	Elvitegravir
1	**02_AG**	**17**		**2,53**	Susceptible	Susceptible	Susceptible	Susceptible
2	**02_AG**	**21**		**2,55**	Susceptible	Susceptible	Susceptible	Susceptible
3	**A6**	**26**	L74I	**2,56**	Susceptible	reduced susceptibility	reduced susceptibility	Susceptible
4	**02_AG**	**20**	N155HN	**2,92**	Intermediate	Resistance	reduced susceptibility	Resistance
5	**A**	**22**	M50IM, L74I	**3,28**	reduced susceptibility	reduced susceptibility	reduced susceptibility	Susceptible
6	**02_AG**	**29**	L74I, T97A, E138K, S147G, N155H	**3,42**	Intermediate	Resistance	reduced susceptibility	Resistance
7	**D**	**23**	V260I	**3,44**	Susceptible	reduced susceptibility	Susceptible	Resistance
8	**A6**	**20**	L74I	**3,55**	Susceptible	reduced susceptibility	reduced susceptibility	Susceptible
9	**A1**	**26**	L74ILM, S119PRST	**3,65**	reduced susceptibility	reduced susceptibility	reduced susceptibility	reduced susceptibility
10	**01_AE**	**18**	L74ILM, T97AT, G163EGKMRV	**3,82**	reduced susceptibility	Resistance	reduced susceptibility	Intermediate
11	**A6**	**25**	L74I	**4,17**	Susceptible	reduced susceptibility	reduced susceptibility	Susceptible
12	**D**	**27**		**4,51**	Susceptible	Susceptible	Susceptible	Susceptible
13	**C**	**22**	L68V, L74I	**4,55**	Susceptible	reduced susceptibility	reduced susceptibility	reduced susceptibility
14	**B**	**24**	L74ILM, S119AGPR	**4,62**	reduced susceptibility	reduced susceptibility	reduced susceptibility	reduced susceptibility
15	**C**	**31**	M50I, L74I, E157Q, V260I	**4,65**	reduced susceptibility	reduced susceptibility	reduced susceptibility	Resistance
16	**C**	**24**		**4,86**	Susceptible	Susceptible	Susceptible	Susceptible
17	**B**	**12**	N155H	**4,97**	Intermediate	Resistance	reduced susceptibility	Resistance
18	**F**	**20**	V260IV	**5,04**	Susceptible	reduced susceptibility	Susceptible	Resistance
19	**B**	**28**	M50IM, L74ILM, S119PRST	**5,15**	reduced susceptibility	reduced susceptibility	reduced susceptibility	reduced susceptibility
20	**B**	**13**	M50IM	**5,35**	reduced susceptibility	Susceptible	Susceptible	Susceptible
21	**C**	**31**	M50I	**5,52**	reduced susceptibility	Susceptible	Susceptible	Susceptible
22	**02_AG**	**22**	L74ILM	**5,68**	reduced susceptibility	reduced susceptibility	reduced susceptibility	reduced susceptibility
23	**A6**	**22**	L74I	**5,70**	Susceptible	reduced susceptibility	reduced susceptibility	Susceptible
24	**B**	**14**	E157Q	**6,03**	reduced susceptibility	reduced susceptibility	Susceptible	reduced susceptibility
25	**B**	**9**	E157Q	**6,03**	reduced susceptibility	reduced susceptibility	Susceptible	reduced susceptibility

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Medical Center for Infectious Diseases, Berlin

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