No impact on HIV-1 quantification by the Alinity m HIV-1 assay due to mutations in the HIV-1 integrase gene

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BACKGROUND

The Alinity m HIV-1 assay (Alinity) is an assay for diagnosing and monitoring HIV-1 infections. It uses a dual target strategy targeting the integrase-gene and the LTR-region. As integrase inhibitors are recommended for initial treatment, the number of drug resistance mutations is increasing. We assessed the impact of multiple mutations in the integrase-gene on HIV-1 quantification by Alinity m HIV-1 in clinical routine.

METHODS

By next generation sequencing we identified 100 samples with at least 5 amino acid changes in the integrase gene with a maximum of 38 amino acids including drug resistance associated positions. Parallel to resistance testing, the viral load had been determined with the Abbott RealTi*m*e HIV-1 assay on the *m*2000 system (*m*2000). Samples were stored at -20°C until retesting on the Alinity m instrument. The HIV-1 subtypes were as follows: A (n=30), B (n=35), C (n=6), CRF01-AE (n=6), CRF02-AG (n=11), G (n=3), others (n=9)

RESULTS

Table 1: Some representative examples of tested HIV-1 samples with integrase-gene mutations

ID	Subtype	all Integrase-mutations (aa 1-288) compared to consenus B	Integrase-Inhibitor resistance associated mutations
Sec235	A	R20K, V31I, S39CS, L45Q, M50R, H51Y, I72V, L74M, I84L, T112V, S119T, T124S, T125A, G134N, K136Q, K160KR, D167E, G193E, V201I, T218I, L234I, W243RW, C280CY, D288N	H51Y, L74M
Sec277	A	K14R, V31I, L45V, S57G, L101I, K111R, T112V, T124A, T125A, G134N, I135V, K136I, D167DE, V201I, I208L, E212A, Q216H, L234I, D253E, S255G, I268L, S283G, R284G, D288N	
Sec335	A6	E11D, R20K, V31I, L45Q, L63V, I72V, L74I, A91T, T112V, S119P, T124S, T125A, G134N, I135V, K136Q, D167E, V201I, T218I, L234I, S255N	L74I
Sec242	B	D25E, S119T, T124N, T125AV, G140GS, Q148HQ, G193E, I208M, N222K, S230N, D232E, L234F, Q252E, D256E, S283G, D288N	G140GS, Q148HQ
Sec303	B	E11D, K14R, S24N, V32I, I72IV, L101I, S119RS, T125A, N155HN, L172I, N222K	N155HN
Sec314	B	E10D, A23AV, L28I, V31I, I60IM, I72V, I113V, T124N, T125A, F181FL, I203IM, A205AT, T206ST, D207DE, K211KR, I220M, Y227F, D256E, A265V	
Sec249	C	E11D, K14R, S24N, D25E, V31I, M50I, I60V, L63LV, I72V, A91G, F100A, L101I, T112V, T124A, T125A, K136Q, V201IV, I208IM, L234I, D256E, R269K, D278A, S283G, R284G, D288N	
Sec330	CRF01_AE	D3E, E11D, R20K, V31I, I72V, L74I, T112V, I113V, S119P, T124S, T125A, G134N, K136Q, V201I, K215N, L234I, N254DN, S255N	L74I
Sec231	CRF02_AG	S17CS, M50IM, I72FIV, F100FL, T124N, T125A, V126L, V151AV, S153AS, A196P, I220IL	V151AV
Sec299	CRF02_AG	K14R, V31I, S39C, L101I, T112V, S119R, T125A, G134N, I135V, K136T, N155HN, V201I, T206S, L234I, R269K, D278DN	N155HN
Sec265	CRF02_AG	K14R, V31I, L74M, L101I, T112V, T124A, T125A, G134N, I135V, K136T, G163E, V201I, T206S, Q214H, L234I, N254K, R269K, V281MV, S283G	L74M
Sec289	CRF68	E11D, A21T, V31I, I72V, T112V, T124N, T125A, G134N, I135V, K136R, D167E, V201I, T206S, K219KN, L234I, V260IV, S283G	V260IV
Sec275	G	S17N, V31I, M50I, I72V, L101I, K111A, T112V, T124A, T125A, G134N, K136T, G149E, V201I, T206S, Y227F, L234I, S255N, D256E, D279G, S283G	
Sec230	CRF02_AG	E11D, V31I, M50I, I72V, A91E, T97AT, L101I, T112V, S119R, T124A, T125V, G134N, K136T, Y143HY, N155HN, E170K, V180I, S195T, V201I, T206S, I208IM, Y227F, L234I, I251IL, N254K, S255G, R269K, S283G	T97AT, Y143HY, N155HN

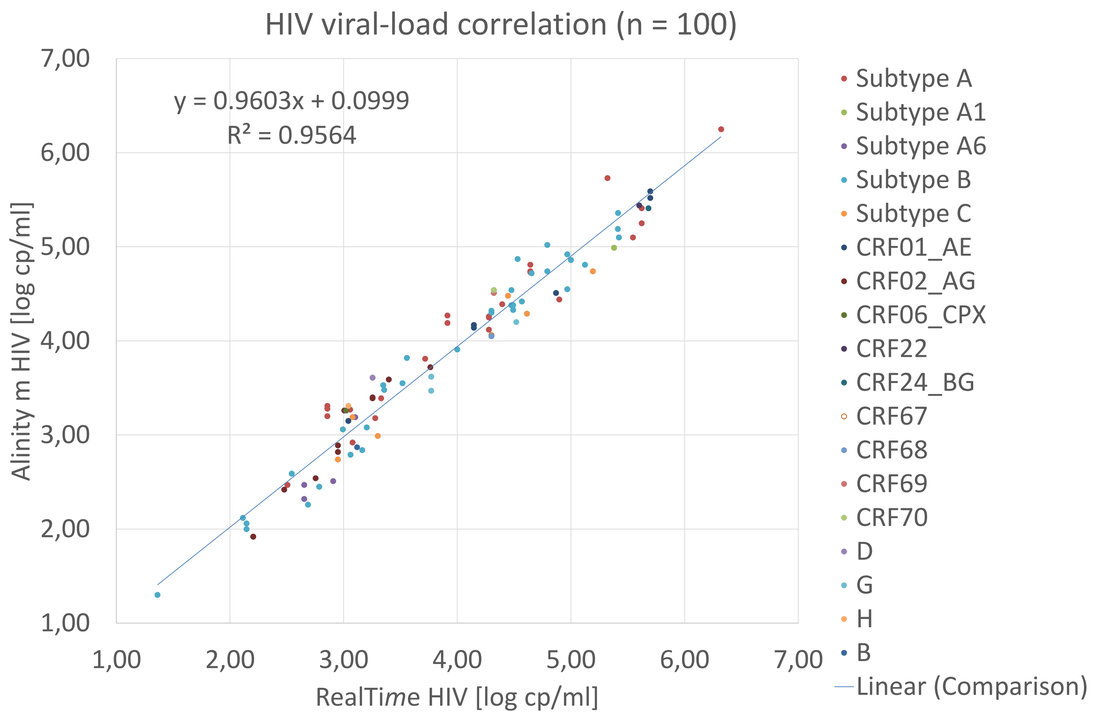

Fig. 1: Correlation of quantitative HIV-1 measurements with the Alinity m and RealTi*m*e in samples with multiple mutations in HIV integrase-gene.

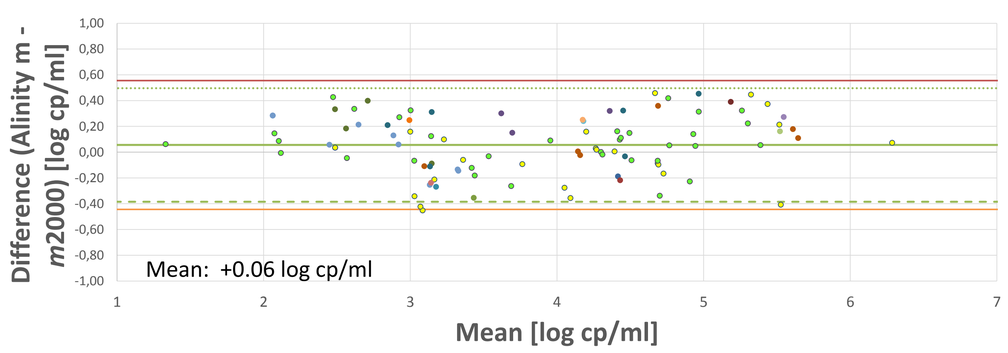

Fig. 2: Bland-Altman plot of HIV-1 measurements with the Alinity m and RealTi*m*e in samples with multiple mutations in HIV integrase-gene.

RESULTS

Mean difference in results was 0.06 log cp/ml. In the Bland-Altman plot, the differences between the two assays were never higher than +/-0.46 log cp/ml. Linear regression showed a coefficient of correlation (Pearson R^2) of 0.96.

CONCLUSIONS

Alinity m and *m*2000 showed high correlation in samples with many mutations in the integrase-gene. Although the *m*2000 is a single target assay we previously showed good correlation to the dual target Aptima™ HIV-1 Quant Dx assay in samples with integrase-resistance mutations. In our hands, also the Alinity m HIV-1 assay proved to be a reliable assay for HIV-1 viral load quantification in diverse subtypes and a substantial amount of mutations in the integrase-gene.

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