Sensitivity and Specificity of a new and high-throughput automated HIV 1/2 Ab/Ag screening assay

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BACKGROUND

Since their introduction in 1985, human immunodeficiency virus (HIV) screening immunoassays based on antibody detection have been continuously improved to shorten the time between HIV infection and its laboratory detection. An early detection of HIV infection is critical for clinical diagnosis and safety of blood products.

Since 1997, more than 10 different HIV combination assays for HIV antigen p24 (Ag) and antibodies (Ab) called fourth-generation assays have been licensed in Europe. These assays reduce the seroconversion window period by 4–8 days when compared to third generation assays, which only detect HIV antibodies.

AIMS

Recently DiaSorin S.p.A. has developed a new fully and high-throughput automated HIV combination assay (up to 171 tests/h): LIAISON® XL murex HIV Ab/Ag HT. The aim of this study was to evaluate the sensitivity and specificity of this new HIV combination assay.

MATERIALS

Sensitivity evaluation

The sensitivity was evaluated with 444 samples in several panels:

- (i) panel 1: 8 samples from HIV-1 p24 Ag reference standard panel with IU/ml from 0 to 20 IU/ml (WHO Ag 90/636) and 7 samples from HIV-1 p24 Ag French reference panel with HIV-1 Ag concentrations from 0 to 200 pg VIH/ml (French Society of Blood Transfusion, SFTS96 HIV-1 p24 Antigen Panel),
- (ii) panel 2: 167 HIV-1 Ab positive samples with known genotypes (157 subtypes HIV-1: 20 A, 21 B, 20 C, 18 D, 17 F, 11 G, 1 H, 3 non B, 20 CRF01_AE, 24 CRF02_AG, 1 CRF06_cpx and 1 CRF11_cpx and 10 HIV-1 group O),
- (iii) panel 3: 95 HIV-1 Ab positive samples and 105 HIV-2 Ab positive samples
- (iv) panel 4: 62 primary HIV-1 infection samples (57 samples p24 Ag positive and Western Blot HIV-1 and HIV-2 Ab negative and 5 samples Ag positive and Western Blot HIV-1 Ab indeterminate).

Specificity evaluation

A total of 769 unselected negative HIV samples (ARCHITECT HIV Combo, Abbott Diagnostics, Delkenheim, Germany) were used. Whenever LIAISON® XL murex HIV Ab/Ag scored reactive, Western blot (NEW LAV Blot I, NEW LAV Blot II; Bio-Rad, Marnes La Coquette, France) and HIV p24 Ag assay (Cobas Core Ag HIV EIA, Roche Diagnostics) were used for confirmation.

RESULTS

Sensitivity for HIV Ag detection

Sensitivity Analysis Using the WHO and SFTS96 HIV-1 p24 Antigen Panel.

The analytical sensitivity of this new assay was 0.531 IU/ml and 9.93 pg/ml as p24 Ag limit of detection (LOD) when using the WHO standard and French national reference panel, respectively.

HIV WHO Standard IU/ml	LIAISON® XL murex HIV Ab/Ag HT S/CO	Abbott HIV Ag/Ab Combo Architect S/CO
0	0.35	0.17
0.5	1.01	0.6
1.0	1.51	0.985
1.5	2.08	1.34
2.0	2.41	1.755
5.0	6.07	4.155
10.0	11.40	8.175
20.0	22.16	17.525

SFTS96 Standard pg/ml	LIAISON® XL murex HIV Ab/Ag HT S/CO	Abbott HIV Ag/Ab Combo Architect S/CO
0	0.37	0.09
5	0.94	0.44
10	1.20	0.63
20	1.53	0.925
50	3.18	1.735
100	5.53	3.55
200	11.72	7.945

S/CO > 1 positive

Detection of p24 Ag HIV-1 in 62 primary infections.

LIAISON® XL murex HIV Ab/Ag HT was positive for all 62 primary HIV-1 infection tested samples.

p24 Ag range (pg/ml)*	Number of samples	Expected positive	LIAISON XL positive results	ARCHITECT positive results
0-10	5	5	5	5
10-50	7	7	7	7
50-100	4	4	4	4
100-500	15	15	15	15
500-1000	10	10	10	10
1000-1500	7	7	7	7
1500-2000	4	4	4	4
2000-4000	2	2	2	2
>4000	8	8	8	8
Total	62	62	62 (100%)	62 (100%)

**VIDAS HIV P24 II (BioMerieux)*

Antibody detection

Sensitivity was 100% (367/367) in antibody positive (HIV-1 Groups M and O, and HIV-2) samples.

HIV-1M Subtype	Number of samples	Expected positive	LIAISON® XL positive results	ARCHITECT positive results
A	20	20	20	20
B	21	21	21	21
C	20	20	20	20
D	18	18	18	18
F	17	17	17	17
G	11	11	11	11
H	1	1	1	1
non-B	3	3	3	3
CRF01_ AE	20	20	20	20
CRF02_ AG	24	24	24	24
CRF06_cpx	1	1	1	1
CRF11_cpx	1	1	1	1
HIV-1 O	10	10	10	10
HIV-1	95	95	95	95
HIV-2	105	105	105	105
Total	367	367	367 (100%)	367 (100%)

Specificity

The diagnostic specificity (769 unselected negative samples) after repeating the initially positive samples was 99.74%

Diagnostic specificity on 769 unselected negative samples

	LIAISON XL			
	Positive	Indeterminate	Negative	Specificity (%)
Initially Positive	3	0	766	99.61
Repeatedly Positive	2*	0	767	99.74

**Western blot HIV1, 2 and Ag p24 Roche: non reactive.*

CONCLUSION

The results of this study showed that the LIAISON® XL murex HIV Ab/Ag HT was highly sensitive with a p24 Ag limit of detection 0.531 IU/ml (WHO p24Ag panel). This new test achieved the 2 IU/mL p24 Ag LOD, fixed by CE (European Community) requirements. And with the specificity 99.7% found in this study, this new assay is well suited for use in HIV diagnostic settings.
In addition it could be a suitable alternative to nucleic acid testing (NAT) for blood donor screening, especially in countries where the incidence of HIV infection is high but NAT screening of blood donors is not feasible or unaffordable.

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