

Evaluation of Antigen and Antibody Sensitivity in 4th Generation HIV Combo Assays Using a Genetically Diverse HIV Panel: ARCHITECT[®] HIV Ag/Ab Combo vs ADVIA Centaur HIV Ag/Ab Combo (CHIV)

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ABSTRACT

Objective:

The use of 4th generation HIV antigen/antibody (Ag/Ab) combination assays has decreased the window between HIV exposure and detection. These assays are designed to detect acute and chronic infections by simultaneously measuring HIV p24 antigen and antibody. Early detection of acute infection is dependent upon antigen sensitivity of the assay, and genetic variation of HIV strains may also impact assay performance. In this study, a genetically diverse panel of HIV virus isolates and HIV-infected plasma was used to compare performance of two 4th generation Ag/Ab combo assays: Abbott ARCHITECT HIV Ag/Ab Combo and Siemens ADVIA Centaur HIV Ag/Ab Combo (CHIV).

Methods:

A panel of 100 unique members representing diluted HIV antigen (n=51) or antibody (n=49) samples including divergent HIV-1 and HIV-2 subtypes and groups as well as 7 seroconversion panels were tested with the FDA approved Siemens ADVIA Centaur HIV Ag/Ab Combo (Centaur CHIV) and Abbott ARCHITECT HIV Ag/Ab Combo (ARCHITECT HIV Combo) assays according to each manufacturer's protocol. Analytical sensitivity of both assays was determined using the WHO International HIV-1 p24 antigen standard.

Results:

ARCHITECT HIV Combo detected all 50 HIV-1 and HIV-2 virus isolate dilutions and 1 diluted antigen only plasma sample, while Centaur CHIV only detected 10 strains, missing 28/35 group M, 9/11 HIV group O, 2 group N and both HIV-2 virus dilutions. In addition, analytical sensitivity of ARCHITECT HIV Combo (0.74 IU/mL) was 2.4-fold better than Centaur CHIV (1.8 IU/ml) based on WHO p24 standard. Of the 49 diluted antibody samples, 47 were ARCHITECT HIV Combo reactive whereas 34 were detected by Centaur CHIV. Two of 34 Centaur CHIV reactive antibody dilutions were not detected by ARCHITECT HIV Combo. Notably, ARCHITECT HIV Combo showed better seroconversion sensitivity than Centaur CHIV, detecting one bleed earlier in 3 of 7 seroconversion panels.

Conclusions:

In comparison with the recently FDA-approved Centaur HIV Combo assay, ARCHITECT HIV Combo demonstrated more sensitive detection of p24 antigen across divergent HIV-1 and HIV-2 strains as well as superior antibody sensitivity for group O and HIV-2 infections.

METHODS

- Identify genetically diverse specimens
 - HIV virus isolates (antigen)
 - HIV-infected plasma samples (antibody)
- Prepare sample dilutions in normal human plasma
- Select commercial HIV seroconversion panels
 - ZeptoMetrix Corporation (n=2)
 - SeraCare (n = 5)
- Reconstitute WHO International Standard HIV-1 p24 Antigen (90/636)
 - Prepare serial dilutions in normal human plasma
- Evaluate samples in 4th generation HIV Combo assays
 - Abbott ARCHITECT HIV Ag/Ab Combo (HIV Combo)
 - Siemens ADVIA Centaur HIV Ag/Ab Combo (CHIV)

PANEL COMPOSITION

Antigen: Virus Isolates	n=51	Subtypes
HIV-1 Group M	35	A, B, C, D, F2, G, CRF01, CRF02, CRF06
HIV-1 Group O	11	
HIV-1 Group N	2	
HIV-1 Group P	1	
HIV-2	2	
Antibody: Plasma	n=49	Subtypes
HIV-1 Group M	21	A, B, C, D, F, G, H, J, CRF01, CRF02, CRF06
HIV-1 Group O	19	
HIV-2	9	
Seroconversion Panels	n=7	46 Bleeds
WHO p24 Ag International Std	n=5	0.312 to 5 IU/mL

RESULTS

HIV Antigen & Antibody Samples

Category	n	Abbott HIV Combo +	Siemens CHIV +
Ag-M	35	35	7
Ag-O	11	11	2
Ag-N	2	2	0
Ag-P	1	1	1
Ag-HIV-2	2	2	0
Ag Total	51	51	10
Ab-M	21	20	15
Ab-O	19	19	14
Ab-HIV-2	9	8	5
Ab Total	49	47	34
Ag/Ab Total	100	98	44

	CHIV +	CHIV -
Ag (n=51)		
ARCHITECT +	10	41
ARCHITECT -	0	0
Ab (n=49)		
ARCHITECT +	32	15
ARCHITECT -	2	0
Ab + Ag (n=100)		
ARCHITECT +	42	56
ARCHITECT -	2	0

- Of the highly diluted virus isolates, ARCHITECT HIV Combo detected 51/51 (100%) and CHIV detected 10/51 (20%).
- Of the highly diluted antibody samples, ARCHITECT HIV Combo detected 47/49 (96%) vs 34/49 (69%) for CHIV.

Seroconversion Panels

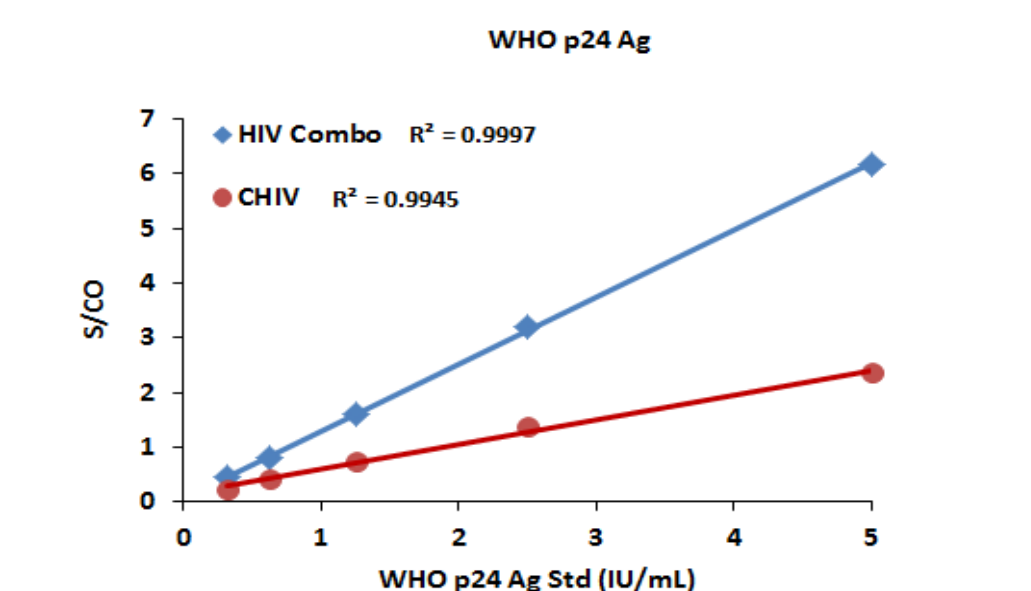
Seroconversion Panel	n	Abbott HIV Combo +	Siemens CHIV +
9014	7	6	5
9089	6	3	3
PRB929	7	5	4
PRB930	4	4	3
PRB932	8	5	5
PRB969	10	3	3
PRB973	4	2	2
Total	46	28	25

SC Panel Member	Viral Load copies/mL	Day Post PCR+	ARCHITECT HIV Combo (S/CO)	CHIV (Index)
9014-1	25,680	0	1.5	0.6
2	5,614	2	0.4	0.3
3	281	10	18.0	1.5
4	<50	12	40.7	1.3
5	<50	24	54.7	3.9
6	<50	29	37.5	4.7
7	<50	31	28.7	5.3
9089-2	<50	-2	0.1	0.1
3	316	0	0.1	0.1
4	146,954	7	4.3	3.1
5	59,647	11	1.0	11.7
6	42,837	15	2.2	>12
PRB932-3	BLD	-14	0.1	0.1
4	400,000	0	14.2	7.2
5	500,000	7	11.5	>12
6	200,000	23	5.3	7.2
8	300,000	136	3.7	5.6
9	70,000	166	3.6	8.3
PRB929-1	Neg	-14	0.1	0.1
2	Neg	-10	0.1	0.1
3	Pos	0	1.2	0.6
4	Pos	4	36.8	>12
5	Pos	7	357	>12
6	Pos	11	464.8	>12
7	Pos	14	107.2	>12
PRB930-1	Pos	0	1.9	0.7
2	Pos	3	8.3	3.1
3	Pos	7	22.6	>12
4	Pos	10	60.2	>12
PRB969-6	16,000	8	0.4	0.2
7	35,000	10	0.8	0.4
8	110,000	17	18.8	>12
9	110,000	19	77.6	>12
10	21,000	24	147.3	6.6
PRB973-1	510	0	0.1	0.1
2	6,400	2	0.4	0.2
3	110,000	7	4.2	1.7
4	840,000	11	24.1	>12

- In 2 of 7 seroconversion panels, ARCHITECT HIV Combo detected two bleeds earlier (3 and 4 days) than CHIV.

WHO International Standard p24 Ag

WHO p24 Ag (IU/ml)	ARCHITECT S/CO	CHIV index
5.000	6.17	2.36
2.500	3.21	1.39
1.250	1.62	0.76
0.625	0.82	0.44
0.312	0.45	0.25
Analytical Sensitivity	0.75 IU/ml	1.85 IU/ml



- Analytical sensitivity with WHO p24 antigen Standard was 2.4-fold more sensitive for ARCHITECT Combo than CHIV.

CONCLUSION

The broad detection of ARCHITECT HIV Ag/Ab Combo across diverse HIV subtypes/groups, when coupled with its high p24 analytical sensitivity and seroconversion sensitivity, indicate that the assay provides more sensitive and accurate detection of HIV infection as compared to Centaur HIV Ag/Ab Combo.

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