HHS Public Access

Author manuscript

J Clin Virol. Author manuscript; available in PMC 2024 April 12.

Published in final edited form as:

J Clin Virol. 2018 July ; 104: 89–91. doi:10.1016/j.jcv.2018.05.005.

Performance of the Alere Determine™ HIV-1/2 Ag/Ab Combo Rapid Test with algorithm-defined acute HIV-1 infection specimens

Monica M. Parker[a], **S. Berry Bennett**[b], **Timothy J. Sullivan**[a], **Sally Fordan**[b], **Laura G. Wesolowski**[c], **Kelly Wroblewski**[d], **Anne M. Gaynor**[d]

[a]Wadsworth Center, New York State Department of Health, 120 New Scotland Avenue, Albany, NY, 12208, United States

[b]Florida Bureau of Public Health Laboratories, 1217 Pearl St., Jacksonville, FL, 32202, United States

[c]Centers for Disease Control and Prevention, United States

[d]Association of Public Health Laboratories, 8515 Georgia Ave., Suite 700, Silver Spring, MD, 20910, United States

Abstract

Background: The capacity of HIV Antigen/Antibody (Ag/Ab) immunoassays (IA) to detect HIV-1 p24 antigen has resulted in improved detection of HIV-1 infections in comparison to Ab-only screening assays. Since its introduction in the US, studies have shown that the Determine HIV-1/2 Ag/Ab Combo assay (Determine Ag/Ab) detects HIV infection earlier than laboratory-based IgM/IgG-sensitive IAs, but its sensitivity for HIV-1 p24 Ag detection is reduced compared to laboratory-based Ag/Ab assays. However, further evaluation is needed to assess its capacity to detect acute HIV-1 infection.

Objective: To assess the performance of Determine Ag/Ab in serum from acute HIV-1 infections. Study design: Select serum specimens that screened reactive on a laboratory-based Ag/Ab IA or IgM/IgG Ab-only IA, with a negative or indeterminate supplemental antibody test and detectable HIV-1 RNA were retrospectively tested with Determine Ag/Ab. Results were compared with those of the primary screening immunoassay to evaluate concordance within this set of algorithm-defined acute infections.

Results: Of 159 algorithm-defined acute HIV-1 specimens, Determine Ag/Ab was reactive for 105 resulting in 66.0% concordance. Of 125 that were initially detected by a laboratory-based Ag/Ab IA, 81 (64.8%) were reactive by Determine Ag/Ab. A total of 34 acute specimens were initially detected by a laboratory-based IgM/ IgG Ab-only IA and 24 (70.6%) of those were reactive by Determine Ag/Ab.

Corresponding author: anne.gaynor@aphl.org.

Conclusions: Due to their enhanced sensitivity, laboratory-based Ag/Ab IAs continue to be preferred over the Determine Ag/Ab as the screening method used by laboratories conducting HIV diagnostic testing on serum and plasma specimens.

Keywords

HIV; acute infection; Determine; algorithm; performance

Background

The Centers for Disease Control and Prevention (CDC) published updated guidelines in 2014 for laboratory diagnosis of HIV in the United States, which recommend use of an HIV-1/2 antigen/antibody (Ag/Ab) combination immunoassay (IA) as the primary screening test in the algorithm [1]. The capacity of Ag/Ab IAs to detect HIV-1 p24 antigen has resulted in a reduction of the diagnostic window period and improved detection of HIV-1 infections in comparison to Ab-only screening assays [2–7]. Identifying individuals with acute HIV-1 infection allows for early treatment, which can reduce transmission, improves health outcomes for infected individuals, and contributes to earlier partner services [8,9]. Of the seven HIV Ag/Ab assays approved by the Food and Drug Administration (FDA) for use in the U.S., six are restricted to laboratory use (laboratory-based). The Determine HIV-1/2 Ag/Ab Combo assay (Determine Ag/Ab) is a single-use rapid test and is CLIA waived for fingerstick whole blood allowing its use in non-laboratory settings. Determine Ag/Ab is also approved for laboratory use with serum, plasma and venous whole blood. Determine Ag/Ab differentiates HIV-1/2 Ab from HIV-1 p24 Ag reactivity. Seroconversion panel studies have shown that the FDA-approved Determine Ag/Ab detects HIV infection in plasma earlier than laboratory-based IgM/IgG sensitive IAs, but its sensitivity is reduced compared to laboratory-based Ag/Ab IAs for both plasma and simulated whole blood [10–12]. However, further evaluation is needed to assess the capacity of Determine Ag/Ab to detect acute HIV-1 infection in serum.

Objective

To assess performance of Determine Ag/Ab in serum specimens identified as acute infections.

Study design

The Association of Public Health Laboratories (APHL) in conjunction with CDC initiated the HIV Nucleic Acid Test Demonstration Project (NAT Demo) in August 2012 to provide access to HIV-1 RNA nucleic acid testing (NAT). The NAT Demo allows PHLs that have specimens with discordant HIV screening and supplemental antibody test results and lack access to HIV-1 RNA testing in-house to resolve the discordance using the recommended algorithm [13]. Specimens submitted to the NAT Demo reference laboratories must be 1) from a US PHL, 2) repeatedly reactive on an FDA-approved laboratory-based Ag/Ab IA or IgM/IgG-sensitive Ab-only screening IA, and 3) negative or indeterminate on a FDA-approved supplemental Ab assay. Diagnostic testing was conducted using one of the following laboratory-based screening assays: Architect HIV Ag/Ab Combo (Abbott

Diagnostics, Chicago, IL), GS HIV Combo Ag/Ab EIA (Bio-Rad Laboratories, Hercules, CA), GS HIV-1/HIV-2 Plus O EIA (Bio-Rad Laboratories), Advia Centaur HIV 1/O/2 Enhanced (Siemens Healthcare Diagnostics, Tarrytown, NY) or VITROS Anti-HIV 1 + 2 assay (Ortho-Clinical Diagnostics, Raritan, NJ). Reactive specimens were tested using one of the following supplemental Ab tests: Multispot HIV-1/HIV-2 Rapid Test (Bio-Rad Laboratories), Geenius HIV-1/2 Supplemental Assay (Bio-Rad Laboratories) or GS HIV-1 Western Blot (Bio-Rad Laboratories). All NAT Demo referral specimens that met the manufacturer's collection and storage requirements were tested with the APTIMA HIV-1 RNA Qualitative Assay (Hologic, San Diego, CA) at either the New York State Department of Health's Wadsworth Center Laboratory (WCL) or the Florida Bureau of Public Health Laboratories (FBPHL). Specimens that screened reactive, had a negative or indeterminate supplemental antibody test and detectable HIV-1 RNA were classified as laboratory algorithm-defined acute HIV-1 infections. Data were not collected regarding whether persons previously knew they were HIV-infected or had received antiretroviral treatment. Sample eligibility criteria were the following: at least 60 μl available, three or fewer freeze-thaws and classified as laboratory algorithm-defined acute HIV-1 based on NAT Demo data. A total of 159 serum specimens submitted between January 2013 and December 2016 met these criteria and were included. Specimens were deidentified and tested in singlet with the FDA-approved Alere Determine HIV-1/2 Ag/ Ab Combo test (Alere Inc., Waltham, MA) according to the manufacturer's instructions. Results of Determine Ag/Ab and the originating laboratory's primary screening immunoassay that identified these laboratory algorithm-defined acute infections were evaluated for concordance. The project was approved as research not involving identifiable human subjects by the Division of HIV/AIDS Prevention at CDC.

Results

Of 159 acute HIV-1 specimens, Determine Ag/Ab was reactive for 105 resulting in 66.0% concordance (Table 1). Determine Ag/Ab reactivity based on HIV-1 antibody detection (Table 1, Ag+/Ab+ and Ag−/Ab+) was 54.7% (87/159) and an additional 11.3% (18/159) were reactive for p24 Ag only.

Of 125 acute specimens initially detected with a laboratory-based Ag/Ab assay, 81 (64.8%) were reactive by Determine Ag/Ab and 44 (35.2%) were nonreactive. A total of 34 acute specimens were initially detected by a laboratory-based IgM/IgG Ab-only IA and 24 (70.6%) of those were reactive by Determine Ag/Ab, with 18 of 24 indicating antibody reactivity (Ag+/Ab+ plus Ag−/Ab+) and 6 indicating HIV-1 p24 antigen detection only. Ten of 34 (29.4%) specimens initially detected by an Ab-only IA were not detected by Determine Ag/Ab (Table 1).

Discussion

In this study, performance of Determine Ag/Ab was assessed retrospectively on serum specimens from individuals with laboratory algorithm-defined acute HIV-1 infection. Determine Ag/Ab failed to detect HIV in 35.2% (44/125) of HIV-1 positive specimens that screened reactive with a laboratory-based Ag/Ab assay. Previously published data on plasma

indicate that the median time to reactivity for Determine Ag/Ab is 2.3–5.5 days earlier than for laboratory-based HIV IgM/IgG Ab-only IAs [12]. However, data from our study indicate that about 30% of acute HIV-1 infections that were detected by a laboratory-based IgM/IgG Ab-only IA would not have been detected if the serum had been screened using Determine Ag/Ab. Of the 24 Determine Ag/ Ab-reactive specimens initially detected by an Ab-only IA, 6 were nonreactive for antibodies, but had detectable p24 antigen by Determine Ag/Ab. For these 6 specimens with discordant antibody results, it is possible that aspects of Determine Ag/Ab's design which differ from instrument-based, antibody-only IAs (e.g. lateral flow format, limited IgM detection, lower specimen testing volume and different antigenic components) could have contributed to this discordance. The presence of multiple envelope, and in some cases p24 core, epitopes in the IgM/ IgG IAs may have allowed antibodies to be detected earlier during seroconversion than the single gp41 protein in Determine Ag/Ab. These data suggest that there may be a window within the seroconversion period in which Ab-only IAs can detect HIV-1 antibodies that are not reliably detected by Determine Ag/Ab.

Although this study provides data on the ability of Determine Ag/Ab to detect HIV-1 in serum collected from individuals with laboratory algorithm-defined acute HIV-1 infection, we do not have data to evaluate concordance between Determine Ag/Ab and laboratory-based IAs in specimens that screened nonreactive with a laboratory-based IA. Determine Ag/Ab may have detected acute HIV-1 infections that were missed by laboratory-based screening IAs, especially when laboratory-based IgM/IgG Ab-only screening IAs were used [10,12]. Our data indicate that the specimen storage conditions were appropriate for maintaining antigen detection, however we cannot exclude the possibility that p24 Ag may have degraded in some specimens during the period after initial screening. Despite the ability of Determine Ag/ Ab to distinguish between p24 Ag and HIV-1/2 Ab reactivity, data from this study indicate that some acute HIV-1 infections will be missed using Determine Ag/Ab. Due to their enhanced sensitivity, laboratory-based Ag/Ab IAs continue to be the preferred screening method for laboratories conducting HIV diagnostic testing on serum and plasma. However, some laboratories may choose to use the Determine Ag/Ab rapid test rather than a laboratory-based Ag/Ab IA for practical reasons including low testing volume, need for quick turnaround and instrumentation costs [14]. Therefore, when reporting negative Determine Ag/Ab results, laboratories should consider informing providers of the assay's reduced sensitivity relative to other FDA-approved HIV Ag/Ab assays and the potential for false negative results during acute HIV-1 infection.

Acknowledgements

This project was 100% funded with federal funds from a federal program of $115,163. This publication was supported by Cooperative Agreement #5NU60OE000103 funded by the Centers for Disease Control and Prevention. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of CDC or the Department of Health and Human Services. No competing interests are declared. Ethical approval was not required. The project was approved as research not involving identifiable human subjects by the Division of HIV/AIDS Prevention at the Centers for Disease Control and Prevention.

References

1. Centers for Disease Control and Prevention and Association of Public Health Laboratories, Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations, (2018) Available at http://stacks.cdc.gov/view/cdc/23447. Published June 27, 2014. (Accessed 12 September 2017).
2. Ly TD, Ebel A, Faucher V, Fihman V, Laperche S, Could the new HIV combined p24 antigen and antibody assays replace p24 antigen specific assays? J. Virol. Methods 143 (2007) 86–94, 10.1016/j.jviromet.2007.02.013. [PubMed: 17395277]
3. Pandori MW, Hackett J Jr., Louie B, et al., Assessment of the ability of a fourth- generation immunoassay for human immunodeficiency virus (HIV) antibody and p24 antigen to detect both acute and recent HIV infections in a high-risk setting, J. 2639–2642, 10.1128/JCM.00119-09.
4. Patel P, Mackellar D, Simmons P, Uniyal A, Gallagher K, Bennett SB, Sullivan TJ, Centers for Disease Control and Prevention Acute HIV Infection Study Group, et al., Detecting acute human immunodeficiency virus infection using 3 different screening immunoassays and nucleic acid amplification testing for human immunodeficiency virus RNA, Arch. Intern. Med. 170 (2010) 66–74, 10.1001/archinternmed.2009.445. [PubMed: 20065201]
5. Masciotra S, McDougal JS, Feldman J, Sprinkle P, Wesolowski L, Owen SM, Evaluation of an alternative HIV diagnostic algorithm using specimens from ser- oconversion panels and persons with established HIV infections, J. Clin. Virol. 52
6. Chen DJ, Yao JD, Comparison of turnaround time and total cost of HIV testing before and after implementation of the 2014 CDC/APHL Laboratory Testing Algorithm for diagnosis of HIV infection, J. Clin. Virol. 91 (2017) 69–72, 10.1016/j.jcv.2017.04.004. [PubMed: 28461133]
7. Marson KG, Marlin R, Phan P, Cohen SE, Jones D, Roemer M, Peters PJ, Haller B, C.D. Pilcher, Real-world performance of the new US HIV testing algorithm in medical settings, J. Clin. Virol. 91 (2017) 73–78, 10.1016/j.jcv.2017.04.003. [PubMed: 28434809]
8. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. , Antiretroviral therapy for the prevention of HIV-1 trans- mission, N. Engl. J. Med. 375 (2016) 830–839, 10.112056/NEJMoa1600693. [PubMed: 27424812]
9. INSIGHT START Study Group, Lundgren JD, Babiker AG, Gordin D, Emery S, Grund B, et al. , Initiation of antiretroviral therapy in early asymptomatic HIV infection, N. Engl. J. Med. 373 (2015) 795–807, 10.1056/NEJMoa1506816. [PubMed: 26192873]
10. Masciotra S, Luo W, Youngpairoj AS, Kennedy MS, Wells S, Ambrose K, et al. , Performance of the Alere Determine™ HIV-1/2 Ag/Ab Combo Rapid Test with specimens from HIV-1 seroconverters from the US and HIV-2 infected individuals from Ivory Coast, J. Clin. Virol. 58 (S1) (2013) 35458, 10.1016/j.jcv.2013.07.002.
11. Masciotra S, Luo W, Westheimer E, Cohen SE, Gay CL, Hall L, et al. , Performance evaluation of the FDA-approved Determine™ HIV-1/2 Ag/Ab Combo assay using plasma and whole blood specimens, J. Clin. Virol. 91 (2017) 95–100, 10.1016/j.jcv.2017.03.019. [PubMed: 28372891]
12. Delaney KP, Hanson DL, Masciotra S, Ethridge SF, Owen SM, Time until emergence of HIV test reactivity following infection with HIV-1: implications for interpreting test results and retesting after exposure, Clin. Infect. Dis. 64–1 (2017) 53–59, 10.1093/cid/ciw666.
13. Wesolowski LG, Wroblewski K, Bennett SB, Parker MM, Hagan C, Ethridge SF, et al. , Nucleic acid testing by public health referral laboratories for public health laboratories using the U.S. HIV diagnostic testing algorithm, J. Clin Virol 65 (2015) 6–10, 10.1016/j.jcv.2015.01.017. [PubMed: 25766979]
14. Centers for Disease Control and Prevention, Technical Update: Use of the Determine HIV 1/2 Ag/Ab Combo Test with Serum or Plasma in the Laboratory Algorithm for HIV Diagnosis, (2018) Available at https://stacks.cdc.gov/view/cdc/48472. Published October 14, 2017. (Accessed 4 December 2017).

Table 1

Determine Ag/Ab results for serum specimens classified as acute HIV-1 infections.

Lab screening assay	Acute specimens N	Determine Ag/Ab Results N (%)				
		Reactive	Analyte-specific reactive results			NR
			Ag+/Ab−	Ag+/Ab+	Ag−/Ab+	
Ag/Ab IA	125	81 (64.8)	12 (9.6)	5 (4.0)	64 (51.2)	44 (35.2)
Ab-only IA	34	24 (70.6)	6 (17.6)	2 (5.9)	16 (47.1)	10 (29.4)
Total	159	105 (66.0)	18 (11.3)	7 (4.4)	80 (50.3)	54 (34.0)

Ag, HIV-1 p24 antigen; Ab, HIV-1/2 antibody; +, Reactive; −, Nonreactive (NR).