Clinical Evaluation of the Determine HIV-1/2 Ag/Ab Combo test

To the Editor—Rosenberg et al recently published a field evaluation in Malawi of the Determine HIV-1/2 Ag/Ab Combo point-of-care test (POCT) showing poor detection of acute HIV infection (AHI) [1, 2]. We conducted a prospective clinical evaluation comparing the Combo POCT with the Abbott Architect [3] fourth-generation laboratory assay and
the Determine HIV-1/2 antibody-only POCT (standard POCT) in high-risk patients attending a UK genitourinary medicine clinic.

Participants were prospectively recruited at the Imperial College Healthcare NHS Trust, London, between October 2010 and May 2011. Eligible participants were from groups at high risk for HIV infection (men who have sex with men, persons from HIV-endemic areas, injection drug users, or partners of persons in these groups), ≥18 years old, and able to provide written informed consent. Participants provided finger-prick specimens for parallel testing by the Combo and standard POCTs and a venous sample for laboratory analysis (Architect assay [3], confirmation of positive results by VIDAS assay). Participants received standard POCT and laboratory results but were blinded to Combo POCT results. Sensitivity and specificity in the diagnosis of HIV infection were calculated for the Combo POCT and standard POCT relative to laboratory assay. Analyses were conducted with Stata software, version 12 (StataCorp). The study was approved by the West London research ethics committee (REC2 reference 10/H0711/64).

Of 1001 participants recruited, 985 had parallel HIV tests performed according to the protocol and were considered within this analysis. Participants could enroll more than once during the study period; 940 of 985 individuals participated once, 21 participated twice, and 1 participated 3 times. None of the repeat testers seroconverted. Of the 985 participants 874 (88.7%) were male; 817 of 874 (93.5%) were men who have sex with men, 153 of 985 participants were from HIV-endemic areas, 5 were injection drug users, and 10 were in another risk group.

Twenty-two of 985 participants were HIV positive by laboratory assay (prevalence, 2.3%), of whom 2 were p24Ag positive and antibody negative. Nineteen of 22 participants were correctly identified as HIV positive by the Combo POCT. One laboratory positive participant was not identified by the Combo POCT, which was read beyond the 10-minute reading interval, invalidating results. In comparison with laboratory assays, 2 participants had a false-negative p24Ag result. Three individuals had a positive p24Ag band by the Combo POCT, but none were confirmed p24Ag positive by laboratory assay; 2 of 3 were antibody negative by laboratory screening, and 1 was antibody positive, with p24Ag not determined by VIDAS testing. In this case, neither antibody titers nor avidity testing results were suggestive of AHI.

The overall sensitivity and specificity of the Combo POCT for HIV diagnosis were 90.5% (95% confidence interval [CI], 69.6%–98.8%) and 99.8% (95% CI, 99.2%–99.9%), respectively (Table 1). Two additional practical problems with the Combo POCT were the narrow reading interval, which was exceeded in 7 of 985 participants (0.7%), and failure of the control line, which occurred in 6 of 985 (0.6%).

The standard POCT correctly identified 20 of 22 HIV-positive cases. There were 2 false-negative HIV test results by the standard POCT, in the 2 participants with detectable p24Ag by laboratory assay only. All participants had the test read within the stated 45-minute reading interval, and the control line failed in 2 of 985 tests (0.2%). There were no false-positive results. The specificity was 100% (95% CI, 99.6%–100%). The Combo and standard POCTs each had 1 indeterminate result, in 2 different participants. In this study, the p24Ag band of the Combo POCT did not identify either of the 2 p24Ag-positive participants and gave false-positive results. This is in agreement with the data of Rosenberg et al [4], but in contrast to initial laboratory validation on stored samples [5, 6]. Additional practical complexities in using the Combo POCT were identified, with increased recording of failure of the control line compared with the standard POCT, resulting in void results. Void results with the Combo POCT have been noted elsewhere, with 1 study [7] reporting void results in 19 of 147 tests (13%). The short reading window of the HIV Combo POCT test invalidated 0.7% of the results, which may cause logistical problems in busy clinical settings. Modifications are currently being made to address this problem.

Parallel screening with a POCT and laboratory assay currently occurs within this genitourinary medicine setting only when results are indeterminate, for confirmation when results are positive, or when symptoms or signs of seroconversion are reported. Both patients positive for p24Ag within this study were asymptomatic, and their infection would ordinarily have been undiagnosed with our current clinical algorithm.

The Combo POCT is a tool designed to extend the detection window for HIV

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**Table 1. Summary of Test Performance**

<table>
<thead>
<tr>
<th>Results (95% CI, %)</th>
<th>Combo POCT</th>
<th>Standard POCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>90.5 (69.6–98.8)</td>
<td>90.9 (70.8–98.9)</td>
</tr>
<tr>
<td>Specificity</td>
<td>99.9% (99.2–99.97)</td>
<td>100.0 (99.6–100)</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>90.5 (69.6–98.8)</td>
<td>100.0 (83.2–100)</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>99.8 (99.2–99.97)</td>
<td>99.8 (99.3–99.97)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; POCT, point-of-care test.

* Binomial exact CIs are provided.

* The sensitivity calculation for the Combo POCT excluded the patient whose result was missed owing to the 10-minute reading window.

* One-sided 97.5% binomial CI.
infection beyond the standard POCT, but it fails to add value because of its limited sensitivity in detecting AHI. The detection of AHI remains critical for limiting onward HIV transmission \[2, 8, 9\], and other options for timely detection therefore need to be explored.

Notes

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