CLINICAL EVALUATION AND METHOD COMPARISON OF NOVEL ASSAYS FOR THE DETECTION OF ANTIBODIES ASSOCIATED WITH CELIAC DISEASE

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KEY MESSAGES

- The Aptiva Celiac Disease IgA and IgG Reagents showed excellent clinical performance
- The Aptiva Celiac Disease IgA and IgG Reagents demonstrated high level of agreement with reference methods

INTRODUCTION

Antibodies to tissue transglutaminase (tTG) and deamidated gliadin peptide (DGP) are important factors in diagnosis of celiac disease (CD). Increased anti-tTG IgA titers can be especially important as suggested by the European Society of Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN), where a titer 10 times the upper limit of normal may consider foregoing invasive intestinal biopsy in diagnosis of CD.[1] This study aimed to compare the performance of novel tTG and DGP assays with a reference method using clinically characterized samples.

METHODS

A total of 461 samples were included in the study, consisting of 161 samples from CD patients, and 290 samples from patients with various other diseases including other gastroenterological conditions. All samples were tested by a novel fully automated particle-based multi-analyte technology (PMAT, research use only, Inova Diagnostics, USA). Additionally, all samples were tested in parallel using FDA-cleared chemiluminescent based assays currently on the market (QUANTA Flash, Inova Diagnostics, USA). Qualitative correlations were calculated, and clinical performance was assessed for each of the analytes.

RESULTS

All Aptiva assays for tTG and DGP showed good clinical performance at the manufacturer's recommended cut-off (Table 1). Receiver operating characteristic (ROC) curve analysis was performed to assess the performance at different thresholds (Figure 1).

Table 1 Clinical performance of Aptiva and QUANTA Flash assays using all samples (n=461).

Analyte	tTG IgA	DGP IgA	tTG IgG	DGP IgG
Aptiva Clinical Performance				
Sensitivity % (95% CI)	93.0 (88.1-95.9)	59.1 (51.6-66.2)	58.5 (51.0-65.6)	83.0 (76.7-87.9)
Specificity % (95% CI)	99.3 (97.5-99.8)	99.3 (97.5-99.8)	100.0 (98.7-100.0)	97.9 (95.6-99.0)
Likelihood ratio+ (95% CI)	134.8 (37.5-491.4)	85.6 (23.7-313.4)	+∞ (44.7-+∞)	40.1 (18.7-87.5)
Likelihood ratio- (95% CI)	0.07 (0.04-0.12)	0.41 (0.34-0.48)	0.42 (0.34-0.49)	0.17 (0.12-0.24)
Odds Ratio (95% CI)	1908.0 (456.3-7773.4)	207.8 (54.9-783.0)	+∞ (105.6 -+)	231.8 (95.7-558.7)
QUANTA Flash Clinical Performance				
Sensitivity % (95% CI)	93.0 (88.1-95.9)	64.9 (57.5-71.7)	43.9 (36.6-51.4)	65.5 (58.1-72.2)
Specificity % (95% CI)	99.0 (97.0-99.6)	98.3 (96.0-99.3)	98.3 (96.0-99.3)	97.6 (95.1-98.8)
Likelihood ratio+ (95% CI)	89.88 (31.0-264.0)	37.65 (16.2-88.4)	25.44 (10.9-60.3)	27.14 (13.3-56.2)
Likelihood ratio- (95% CI)	0.07 (0.04-0.12)	0.36 (0.29-0.43)	0.57 (0.50-0.65)	0.35 (0.29-0.43)
Odds Ratio (95% CI)	1267.6 (367.7-4292.5)	105.45 (42.3-262.0)	44.5 (18.0-110.2)	76.8 (34.52-170.1)

Additionally, excellent qualitative agreement was found between the PMAT assays and reference method (Table 2). The results derived from the method comparisons and the clinical evaluation are summarized in the table below.

Table 2 Method comparison of the Aptiva with QUANTA Flash assays using all samples (n=461)

Analyte	tTG IgA	DGP IgA	tTG IgG	DGP IgG
NPA % (95% CI)	99.7 (98.1-99.9)	99.4 (97.9-99.8)	95.1 (92.4-96.9)	93.9 (90.8-96.0)
PPA % (95% CI)	98.8 (95.6-99.7)	87.1 (79.8-92.0)	90.1 (82.3-94.7)	97.7 (93.5-99.2)
TPA % (95% CI)	99.3 (98.1-99.8)	96.3 (94.2-97.7)	94.1 (91.6-95.9)	95.0 (92.6-96.7)
Kappa (95% CI)	0.99 (0.97-1.00)	0.90 (0.85-0.95)	0.82 (0.76-0.89)	0.88 (0.84-0.93)

NPA=Negative Percent Agreement, PPA=Positive Percent Agreement, TPA=Total Percent Agreement

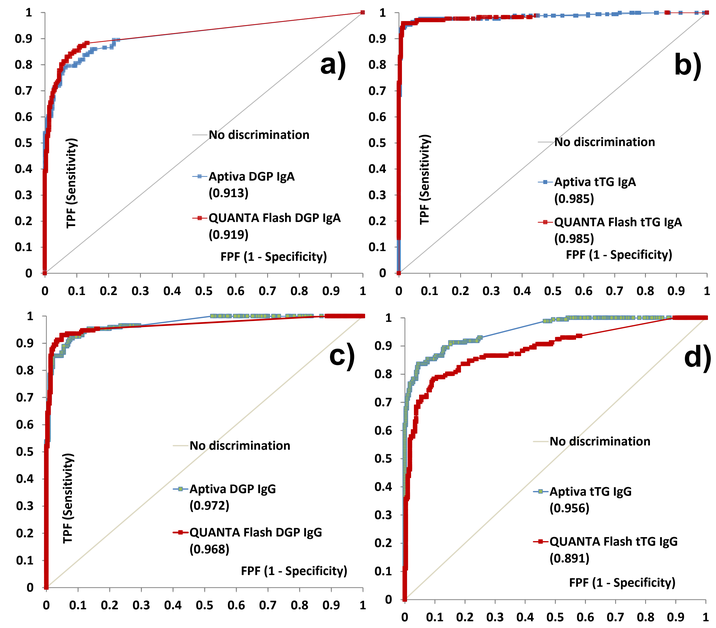
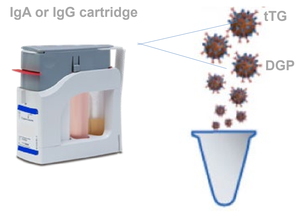


Figure 1 Receiver operating characteristic (ROC) curve analysis for a) DGP IgA (a), tTG IgA (b), DGP IgG (c), and tTG IgG (d) for Aptiva and QUANTA Flash using all samples (n=461).



CONCLUSION

Our data show excellent agreement between the novel PMAT assays and the reference methods. Additionally, all analytes in the novel Aptiva Celiac Disease IgA and IgG Reagents showed excellent clinical performance.

REFERENCES

1. Lakos G, Norman GL, Mahler M, Martis P, Bentow C, Santora D, Fasano A. Analytical and clinical comparison of two fully automated immunoassay systems for the diagnosis of celiac disease. *J Immunol Res* 2014;2014:371263.

2. Walker-Smith JA, Guandalini S, Schmitz J, et al. Revised criteria for diagnosis of celiac disease: Report of working group of European Society of Pediatric Gastroenterology and Nutrition (ESPGAN). *Arch Dis Child* 1990, **65**:909-11.