

# EVALUATION OF EBV ASSAYS (VCA/EA IGG, EBNA IGG AND VCA IGM) ON VIDAS®

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## INTRODUCTION

Epstein Barr Virus (EBV) is a member of the herpes virus family that causes acute mononucleosis and is a candidate causative agent for many human cancers, including Burkitt and Hodgkin lymphomas, some diffuse large B-cell lymphomas and immunodeficiency-associated lympho-proliferative disorders.

After initial infection, the virus becomes latent and can reactivate later in life causing various diseases<sup>1</sup>. Acute infection with EBV can vary widely with regard to the severity and presentation of illness, ranging from an asymptomatic infection to a serious, life-threatening version of mononucleosis<sup>1</sup>. The variety of symptoms and overlap with other viral infections underscore the importance of laboratory testing in the diagnosis of acute EBV-related disease.

Serological markers for EBV infection have been, and remain the most commonly diagnostic tools used for this purpose. Several analytical methods (IFA, EIA, immunoblot, etc.) have been developed for each major serological marker (VCA IgG and IgM; EBNA IgG; EA IgG; heterophilic antibodies) and many comparative studies have been conducted.

**The aim of this study was to evaluate the performance (sensitivity and specificity) of Vidas® (bioMérieux) EBV assays (VCA/EA IgG, EBNA IgG and VCA IgM) and to compare them with the performances of ImmunoWELL™ (GenBio) EBV assays (VCA IgG, EBNA IgG and VCA IgM), that are currently used in our laboratory.**

## MATERIAL AND METHODS

One hundred and eight sera were tested with Vidas® (bioMérieux) EBV assays (VCA/EA IgG, EBNA IgG and VCA IgM) and with ImmunoWELL™ (GenBio) EBV assays (VCA IgG, EBNA IgG and VCA IgM). When results were discordant, sera were analysed also with ImmunoDOT™ (GenBio). For these samples, serological status was defined following the 2 out of 3 statistical method.

## RESULTS

The serological profile of 89 out of 108 sera was similar (table 1). Results of 19 sera were discordant for one marker (table 2). Following standard rules<sup>2</sup>, the overall interpretation of 11 sera was similar between the two test. Six sera had at least one profile with the three positive markers (in five cases with the test ImmunoWELL™). In these cases the clinical attitude was to request a second sample, which helped to define the exact serological status (Data not shown). Two samples showed a discordance that could be significant (all markers negative except the VCA IgG with ImmunoWELL™). This discordance could lead to different clinical interpretation (past infection vs. EBV naive). However, the values were very close to the threshold and it is reasonable to consider that correct attitude is to test a second sample 2-3 weeks later for a final serological interpretation. Therefore, no relevant discordances were observed between the two EBV assays.

On the basis of the chosen criteria (concordance with the results of the test ImmunoWELL™ or the rule of 2 out of 3 concordant results), the relative sensitivities of the tests performed with Vidas® were of 99% (VCA/EA IgG), 100% (EBNA IgG) and 100% (VCA IgM) (table 3). The relative specificities were of 90% (EBNA IgG) and 99% (VCA IgM). The relative specificity of the test combined VCA/EA could seem low (88%), but it is certainly the consequence of a faster positivity of the test during early infection compared to the marker VCA IgG of ImmunoWELL™. Indeed, the marker VCA/EA IgG allowed earlier detection of IgG in 5 of 12 (42%) acute infections (table 2).

**Table 1: similar serological profiles (89 out of 108 samples)**

Vidas®	Serological markers			Number in study
	VCA/EA IgG	EBNA IgG	VCA IgM	
ImmunoWELL™	VCA IgG	EBNA IgG	VCA IgM	
	neg	neg	neg	8
	POS	neg	POS	7
	POS	POS	neg	70
	POS	neg	neg	3
	neg	POS	neg	1

**Table 2: list of discrepant results**

ImmunoWELL™				Number in study	Vidas®			Remarks
VCA IgG	EBNA IgG	VCA IgM	VCA/EA IgG		EBNA IgG	VCA IgM		
neg	neg	POS	POS	5	POS	neg	POS	
POS	neg	POS	neg	1	neg	neg	POS	
POS	POS	POS	POS	4	POS	neg	POS	Dot EBNA IgG negative
POS	POS	POS	POS	1	POS	POS	neg	Dot VCA IgM negative
POS	POS	Neg	POS	1	POS	POS	POS	Dot VCA IgM negative
POS	neg	neg	POS	3	POS	POS	neg	
POS	POS	neg	neg	1	neg	POS	neg	
POS	neg	neg	neg	2	neg	neg	neg	VCA IgG near the cut off
POS	POS	neg	POS	1	POS	neg	neg	

**Table 3: Relative sensitivity and specificity**

	VCA / VCA IgG	EBNA IgG	VCA IgM
<b>Sensitivity</b>	99%	100%	100%
<b>Specificity</b>	88%	90%	96%

## CONCLUSION

Our study focused on a panel of 108 samples from patients with serological status classified as "EBV naive", "acute infection" and "past infection". We observed that:

- no discordances with significant clinical relevance were present;
- relative sensitivity and specificity were consistent with the data described in the literature and in agreement with the diagnosis requirements;
- the combined VCA/EA IgG test is useful for detection of early infections

**In our study, the Vidas® EBV assays showed good performances and we can conclude that they are a reliable alternative for laboratories.**

## REFERENCES

1. **Johannsen E. C. et al.** Epstein-Barr Virus (Infectious Mononucleosis), p. 1801-20. In Mandell G. L. et al. Principles and Practice of Infectious Diseases, 6th ed., vol. 2. 2005, Elsevier.
2. **Klutts JS et al.** Evidence-based approach for interpretation of Epstein-Barr virus serological patterns. *J Clin Microbiol.* 2009; 47:3204-10.