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Evaluation of the new LIAISON® CMV IgG, IgM and IgG Avidity II assays

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OBJECTIVE

Accurate diagnosis of Cytomegalovirus (CMV) infection is important, especially in pregnancy and immunocompromised patients. The aim of this study was to compare diagnostic performances of the new LIAISON® CMV II line with the routine methods used in the laboratory. The performance of the assays, run on the fully automated random access LIAISON® XL analyser, was assessed for the ability to discriminate between samples from subjects not previously infected by CMV, those that have had previous contacts with CMV and patients that experienced CMV primary infection.

METHODS

LIAISON® CMV IgG II is a indirect chemiluminescent immunoassay intended for the quantitative determination of IgG antibodies to CMV in human serum and plasma.
LIAISON® CMV IgM II is a indirect chemiluminescent immunoassay intended for the semi-quantitative determination of IgM antibodies to CMV in human serum and plasma.
LIAISON® CMV IgG Avidity II is a chemiluminescent immunoassay intended for the determination of antigen-binding avidity of IgG antibodies to CMV in human serum and plasma, comparing the signal of untreated sample with the signal of the same sample after treating with urea.
Results obtained with LIAISON® CMV II IgG and LIAISON® CMV IgG Avidity II were compared to those obtained with VIDAS CMV IgG and VIDAS CMV IgG Avidity.
Results obtained with LIAISON® CMV II IgM were compared with those obtained with ETI-CYTOK-M reverse Plus run on ETI-Max 3000. VIDAS IgM was also used in case of discordant results.
All assays were performed according to the recommendations of the manufacturers. The study was performed with 160 residual specimens from prospective population (routine samples) and 191 retrospective selected samples.

According to the results obtained with the serological methods used in the laboratory as well as additional clinical and diagnostic data, selected sera were classified in 5 groups:

- **84 sera from 36 seroconverting patients:** sequential sera from patients with recent infection defined as appearance of IgG in a patient known to be previously negative and presence of IgM, or presence of IgM with increasing IgG or low avidity of IgG. For 17 patients, a first IgG and IgM negative sample was available and tested.
- **35 seronegatives:** defined as IgG and IgM negative
- **35 past infections:** defined as IgG positive and IgM negative
- **20 long lasting IgM:** defined as presence of IgM with ETI-CYTOK-M reverse Plus for more than one year. All these samples show positive IgG.
- **17 IgM EIA false positives:** defined as with ETI-CYTOK-M reverse Plus positive,VIDAS IgM negative.

RESULTS

ROUTINE SAMPLES

Comparison between LIAISON® CMV II assays and the reference methods on the routine population showed an overall agreement of 98.8% for the IgG and 98.1% for the IgM:

Table1: Comparison of LIAISON® and VIDAS CMV IgG assays

LIAISON® CMV IgG II \ VIDAS CMV IgG	Positive	Negative	Total
Positive	89	0	89
Negative	2*	69	71
Total	**91**	**69**	**160**

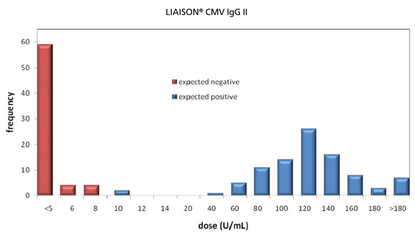
*Same patient, seroconversion of IgG without IgM post-liver/kidney transplantation. CMV PCR negative.

Table 2: Comparison of LIAISON® and ETI CMV IgM assays

LIAISON® CMV IgM II \ ETI-CYTOK-M	Positive	Equivocal	Negative	Total
Positive	1	0	2**	3
Equivocal	0	0	3***	3
Negative	2*	1***	151	155
Total	**3**	**1**	**156**	**160**

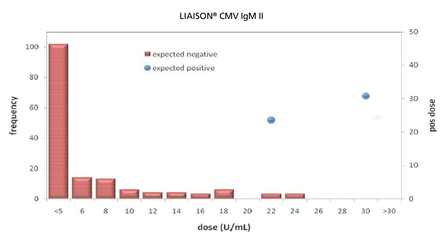
* 1 RF interference, 1 false positive EIA (VIDAS neg); ** 1 primary infection 3 months before, 1 false positive (VIDAS neg); *** false positives (VIDAS neg)

Figure 1:
LIAISON® CMV IgG II samples U/mL distribution:



Assay range: 5-180 U/mL
Interpretation of results: <12 U/mL: negative 12-14 U/mL: equivocal ≥14 U/mL: positive

Figure 2:
LIAISON® CMV IgM II samples U/mL distribution:



Assay range: 5-140 U/mL
Interpretation of results: <18 U/mL: negative 18-22 U/mL: equivocal ≥22 U/mL: positive

SEROCONVERSION SAMPLES :

As shown in table 3 and 4, comparison between LIAISON® CMV II assays and the reference methods showed an overall agreement of 92.9% for the IgG and 86.9% for the IgM. The discrepant results can be generally explained by close timing of the follow-up or by the different ability to identify persistent IgM

Table 3: Comparison of LIAISON® and VIDAS CMV IgG assay

LIAISON® CMV IgG II \ VIDAS IgG	Positive	Equivocal	Negative	Tot
Positive	60	0	2	62
Equivocal	2	0	0	2
Negative	1	1	18	20
Total	63	1	20	84

Agreement: 92.9 %

Table 4: Comparison of LIAISON® and ETI CMV IgM assay

LIAISON® CMV IgM II \ ETI-CYTOK-M	Positive	Equivocal	Negative	Tot
Positive	63	1	2	66
Equivocal	5	0	0	5
Negative	3	0	10	13
Tot	**71**	**1**	**12**	**84**

Agreement: 86.9 %

Avidity was performed on 37 samples and showed a good agreement with VIDAS and/or clinical data. Comparison with VIDAS was limited to 10 samples so no conclusion can be drawn. Comparison with VIDAS needs further investigations. However on sequential samples, LIAISON® IgG avidity showed a good agreement with timing from first withdrawal, as shown in figure 3.

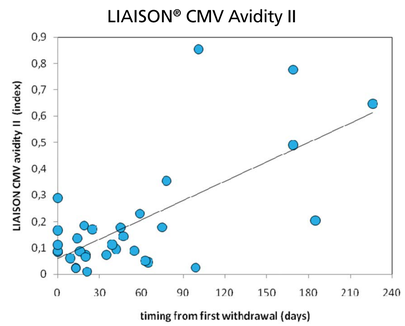


Figure 3:
LIAISON® CMV Avidity Index according to timing from first withdrawal

SERONEGATIVE SAMPLES:

100% agreement on both IgG and IgM was observed on these 35 samples. All IgG dosage showed a result <5 U/mL. For IgM, 23 samples showed a result <5 U/mL, 12 results ranged between 5.04 and 15.5 u/mL.

PAST INFECTIONS:

We observed a 94.3% agreement for IgG on these 35 samples: 2 sera expected to be positive were classified as negative with LIAISON® XL (8.65 and 8.42 U/mL). The first sample belongs to the same transplanted patient described in table 1. The second belongs to a transfused lungs transplanted patient who was tested CMV IgG negative with VIDAS one year later. In this case, we can assume that the IgG detected by VIDAS are those acquired from transfusion. 97.1% agreement for IgM was observed: 1 sample expected to be negative was found equivocal with LIAISON® XL.

LONG LASTING IgM SAMPLES:

On the 20 samples with persistent IgM detected by EIA, we found 10 positive, 6 equivocal and 4 negative results with LIAISON® XL. 19 out of these 20 samples showed high avidity results, which matched the expected results based on clinical data. One sample showed a moderate avidity but was LIAISON® IgM negative.

IgM EIA FALSE POSITIVE SAMPLES:

16 out of 17 samples known to show false positive IgM by EIA were assessedcorrectly as negative by the LIAISON® assay. We also tested IgG on these samples and agreement was 100%: 13 positive and 4 negative.

CONCLUSIONS

The performances of the fully automated LIAISON® CMV II line assays are comparable to those of the reference methods used in the lab for both prospective and selected populations. This new CMV line is a useful tool for the diagnosis of CMV infections and CMV immune status in clinical settings.

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