QuantiFERON®-CMV assay and TTV viremia in prediction of cytomegalovirus reactivation in R+ kidney transplant recipients

Sarah MAFI[1-2], Françoise GARNIER-GEOFFROY[3], Sébastien HANTZ[1-2-3], Sophie ALAIN[1-2-3] and French CMV study group

[(1)] Univ. Limoges, UMR 1092, Limoges, France; [(2)] INSERM, UMR 1092, Limoges, France ; [(3)] National Reference center for Herpesviruses, Virology department, CHU Limoges, Limoges, France

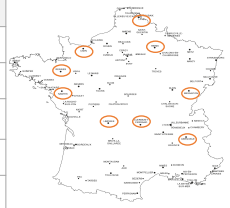
OBJECTIVES

Monitoring CMV-specific cell-mediated immunity by the QuantiFERON®-CMV assay (QF) has been shown to be particularly useful in predicting the risk of CMV infection in kidney transplant recipients (KTR). TTV viremia has also been proposed as a biomarker of immune status in KTR. This study evaluates the ability of the QF and TTV viremia to predict CMV reactivation during the first year of transplantation in R+ KTR.

STUDY POPULATION

A French prospective multicenter (n=9) observational study was conducted on 64 R+ KTR between 2013 and 2017.

Baseline characteristics of the study population	
Age (years; mean ± SD)	54.4 ± 13.5
Male	42 (66%)
CMV status: D+/R+ ; D-/R+	28 (44%) ; 36 (56%)
CMV prophylaxis	44 (69%)
Duration of prophylaxis (months; ± SD)	4.3 ± 1.9



METHODS

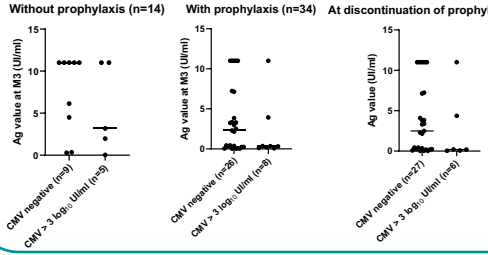
QF, TTV and CMV viral loads were performed before transplantation (J0) and from month (M) 1 to M12 after transplantation.

Quantitative values of the Ag (QF CMV T-cell specific response), Mg (QF global T-cell response) and TTV viremia were compared between CMV negative and CMV > 3 log IU/ml patients. These analyses were performed at M3 and at discontinuation of prophylaxis for each patient.

A qualitative analysis was carried out using the 0.2 IU/mL, 0.5 IU/mL and 3 log cp/ml cut-offs for Ag, Mg and TTV respectively. For markers performance evaluation, sensitivity, specificity, positive and negative predictive values (PPV and NPV) were calculated.

RESULTS

27 patients developed CMV infection during follow-up and 15 of them exhibited a load > 3 log IU/ml. Mean TTV load peaked at M3 then decreased from M3 to M12. Both mean values of Ag and Mg decreased from J0 to M1.



QUANTITATIVE ANALYSIS

The median of Ag at M3 as well as the median of Ag at discontinuation of prophylaxis were notably higher in CMV-negative patients than in CMV > 3 log IU/ml patients, although statistically non-significant with Fisher's test (small numbers analyzed, few CMV infections > 3 log IU/ml)

Similar results for Mg and TTV at M3 were obtained.

QUALITATIVE ANALYSIS

Prediction of CMV infection between M2 and M12 with a non-reactive Ag (< 0.2 IU/ml) or a non-reactive Mg (< 0.5 IU/ml) or/and a TTV viremia > 3 log cp/ml at M1 :

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Individual marker analysis:				
Antigen	28	**81**	46	**67**
Mitogen	30	**82**	50	**67**
TTV	**67**	32	36	**63**
Combined analysis of markers:				
Antigen + TTV	24	**84**	45	**66**
Mitogen + TTV	24	**92**	63	**67**

CONCLUSION

QF and TTV at M3 or Ag value at cessation of prophylaxis do not appear to be sufficient to predict CMV reactivation and to adapt antiviral prophylaxis in R+ KTR. They are more predictive of CMV viremia control than reactivation (NPV > NPP). TTV viremia at M1 seems to be a relevant indicator of immunosuppression in patients with CMV reactivation (sensitivity of 67%). QF in combination with TTV viremia at M1 provides greater specificities and may be useful to identify patients at lower risk of CMV reactivation.