# SUBCLINICAL GRAFT REJECTION AND LOWER TTV VIRAL LOAD IN RENAL TRANSPLANT PATIENTS

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#### Introduction

- Graft and patient survival are mainly determined by rejections and infectious complications in transplant recipients.
- Subclinical graft rejection (SGR) is defined histologically as acute rejection characterized by tubule-interstitial
  infiltration of the renal allograft without clinical deterioration.
- The nonpathogenic, highly prevalent Torque Teno Virus (TTV) has been proposed as biomarker of immunosuppression in transplant patients.

## **Objectives**

- To determine clinical and subclinical graft rejection frequency up to 12 months post-transplantation.
- To determine the association between SGR and TTV viral load in renal transplant patients.



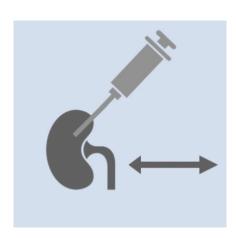
#### **Materials and Methods**



**CEMIC** 2018-2021



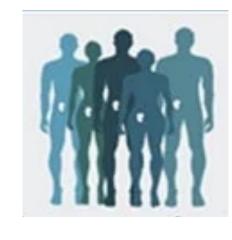
135 KTx 2018-2021



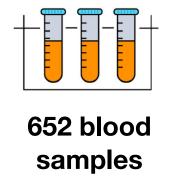
3 - 6 months9 - 12 months



**SGR** 



**Control Group: No AR - No Infection** 





TTV Comercial Kit\*
R-GENE®PCR

- TTV viral load was determined in plasma samples collected before and after renal transplantation using R-GENE®PCR kit (bioMérieux, Marcy-l'Etoile, France).
- The last sample before renal biopsy was analyzed.
- TTV viral loads from patients with SGR and patients without graft rejection or viral infection (control group) were compared.



#### Results

Recipients characteristics		
Age, years old [mean ± SD]	49.2 ± 14.0	
Gender (male ) [n (%)]	61 (63.5)	
Hemodialysis [n (%)]	82 (85.4)	
Time on dialysis, months [median (IQR)]	32.1 (18.0-62.3)	
Donor characteristics		
Living donor [n (%)]	25 (26.0)	
Donor age, years old [mean ± SD]	44.9 ± 17.7	
Donor gender (male ) [n (%)]	50 (52.1)	
Transplant characteristics		
First transplant [n (%)]	85 (88,5)	
Donor Specific Antibody [n (%)]	8 (8.3)	
ATG induction [n (%)]	95 (98.9)	
Tacrolimus, mycophenolic acid and steroids maintenances [n (%)]	96(100%)	
DGF [n (%)]	22 (22.3)	
Miss match [median (IQR)]	4 (3-5)	

Data from 92/96 patients were analyzed.

- → 4 patients died because of infections
  - 1 measles encephalitis, 1 bacterial septicemia and 2 severe COVID

# Renal Biopsies (protocol and indication): 135

- → Graft Rejection (clinical & SCR): 28/92 (30%).
- → SCR: 10/92 (10%).



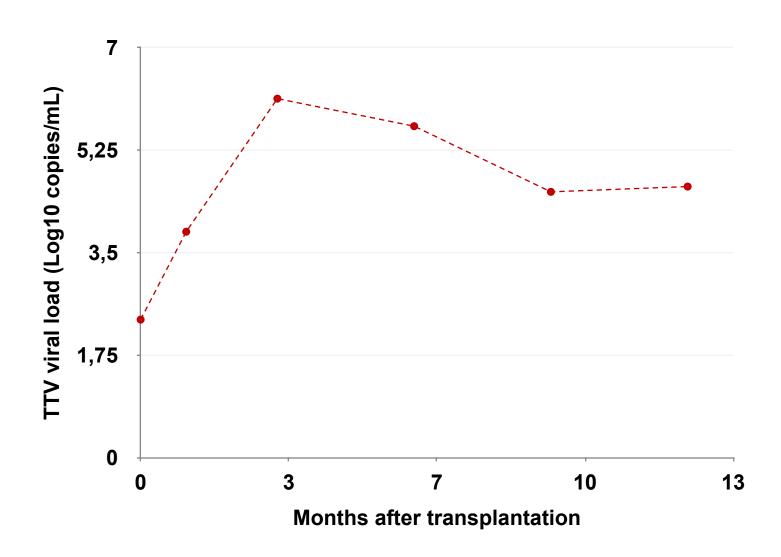
Type of Rejection				
TCMR	7			
BL	2			
ABMR	1			

All patients remained with a functional graft.



### Results

#### • Fig 1. TTV viral load kinetics



TTV viral load increased after transplantation, reaching the peak at month 3. Afterwards, it slightly decreased and reached a plateau.

#### • Fig 2. TTV viral load & SCR

			TTV MEDIAN VIRAL LOAD (IQR)			
n patients		F	R-GENE®PCR			
Months post- transplantation	SGR	Control Group	SGR	Control Group	p value	
3-6	4	44	4.8 (3.7 - 6.8)	6.1 (5.0 - 7.0)	0.360	
6-9	4	29	2.4 (0.5 - 4.8)	6.0 (4.3 - 7.0)	0.017	
12-15	2	22	3.6 (2.6 - 4.6)	5.0 (3.8 - 6.3)	NA	

NA: not applicable

Between months 6-9 post-transplantation, TTV viral load was significant lower in patients with SGR (2.4  $Log_{10}$  copies/mL) compared to control group patients (6.0  $Log_{10}$  copies/mL) (p=0.017).



#### Conclusion

- Graft rejection (clinical and subclinical) occurred in 30% of our cohort.
- Specifically, a third of them had a SGR.
- TTV viral load was significant lower in patients with SGR compared to control group patients at 6-9 months post-transplantation.
- TTV could be used as an early biomarker to identify patients at higher risk of developing SGR.

• We are very grateful to Philippe Bourgeois and Carole Janis for all the support and effort in providing the TTV R-GENE® kits and we want to thank all the hospital staff involved.

