

Factors influencing Torque Teno Virus (TTV) viral load in a sizable population of solid organ transplant recipients

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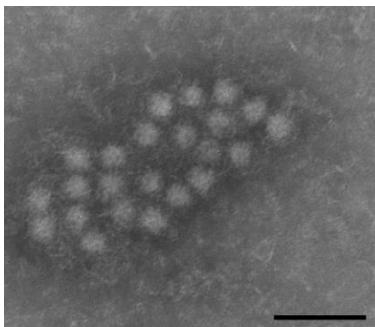
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de Microbiologie





Conflicts of interest



INTRODUCTION

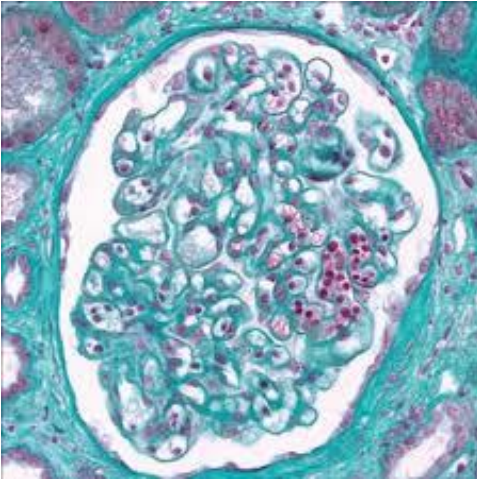
I have no conflicts of interest to disclose.

Immune monitoring:

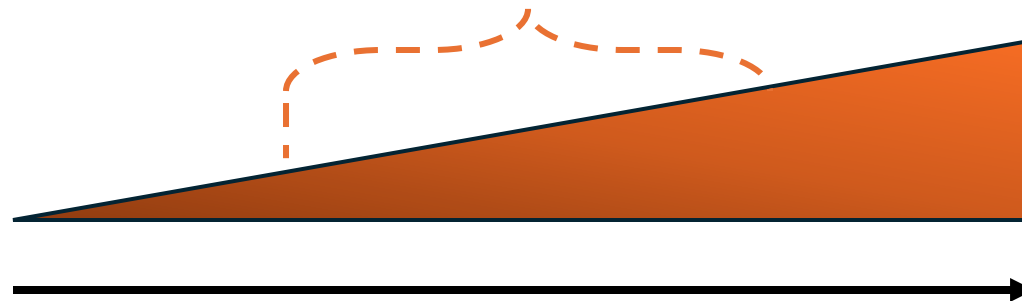
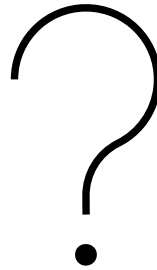
Finding the ideal biomarker: a great challenge



INTRODUCTION



REJECTION



DEGREE OF IMMUNOSUPPRESSION



CANCER
&
INFECTION



Anellovirus :



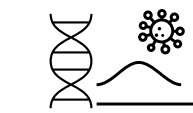
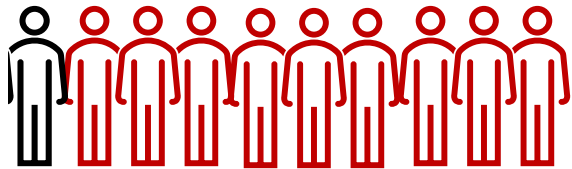
Infection < 4 years

Respiratory transmission

Feco-oral transmission

Blood transmission

Ubiquitous, **Prévalence 90%**



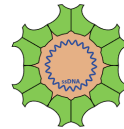
PCR

R-GENE®

10¹ à 10¹⁰ cp/ml

5'UTR

ORF2



Torque: Circular ss-DNA

Teno: Small size 3,6 kb

Virus: Orphan

ORF1



INTRODUCTION



Immune-controlled replication

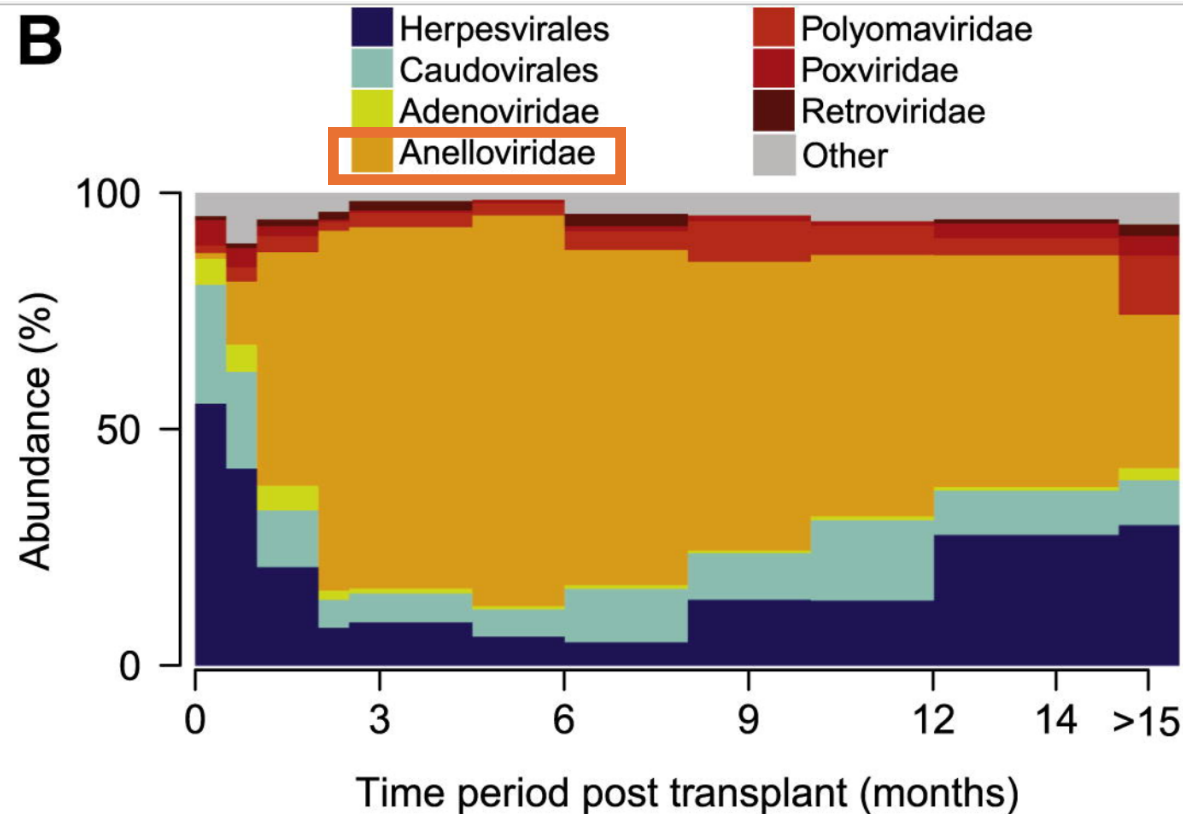


Torque Teno Virus:

The main component of the virome in transplant recipients



INTRODUCTION



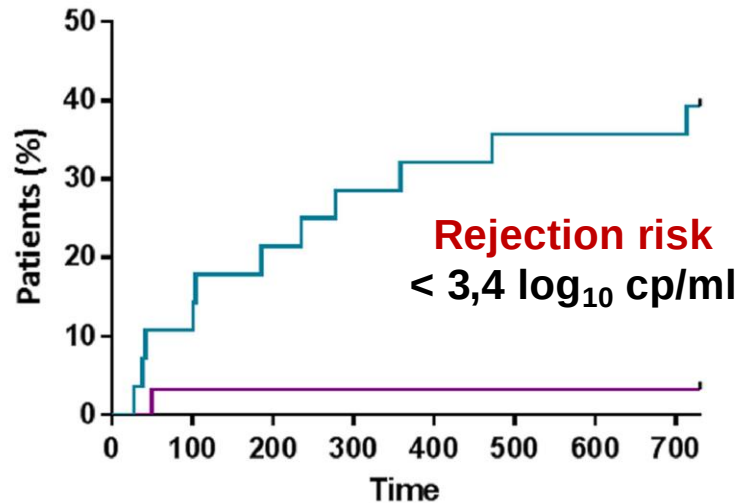
De Vlaminck, Cell, 2013

TTV VL a tool for predicting adverse events



INTRODUCTION

Graft rejection

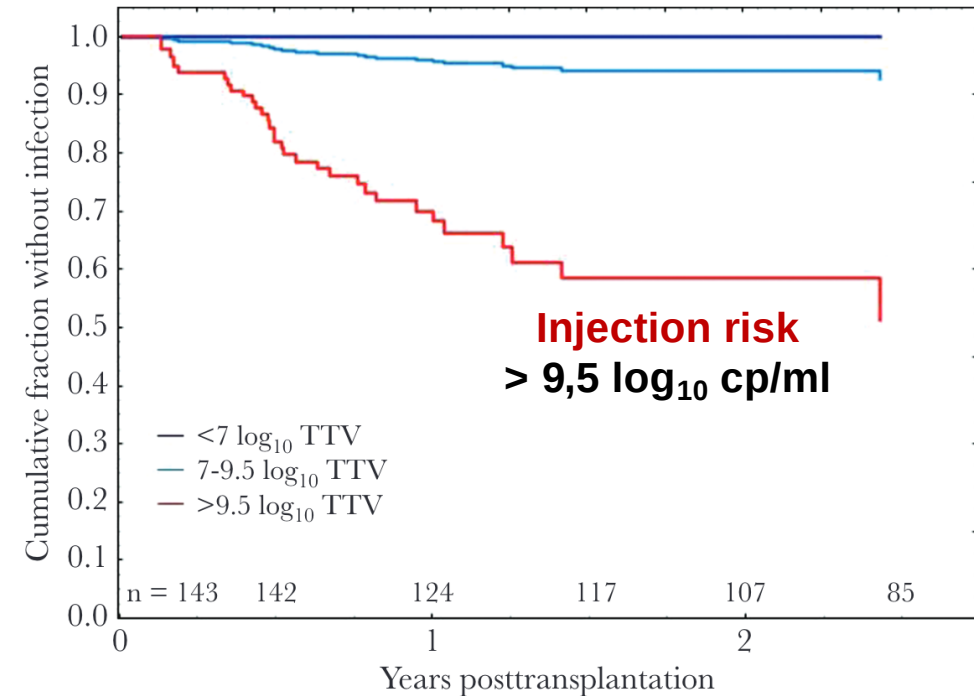


TTV < 3,4 log ₁₀ cp/ml	28	25	22	20	19	18	18	17
TTV > 3,4 log ₁₀ cp/ml	31	30	30	30	30	30	30	30

- TTV load < 3.4 log₁₀ copies/ml
- TTV load > 3.4 log₁₀ copies/ml



Solis M et al, J. Infect. 2019



Jaksch P et al, JID 2018

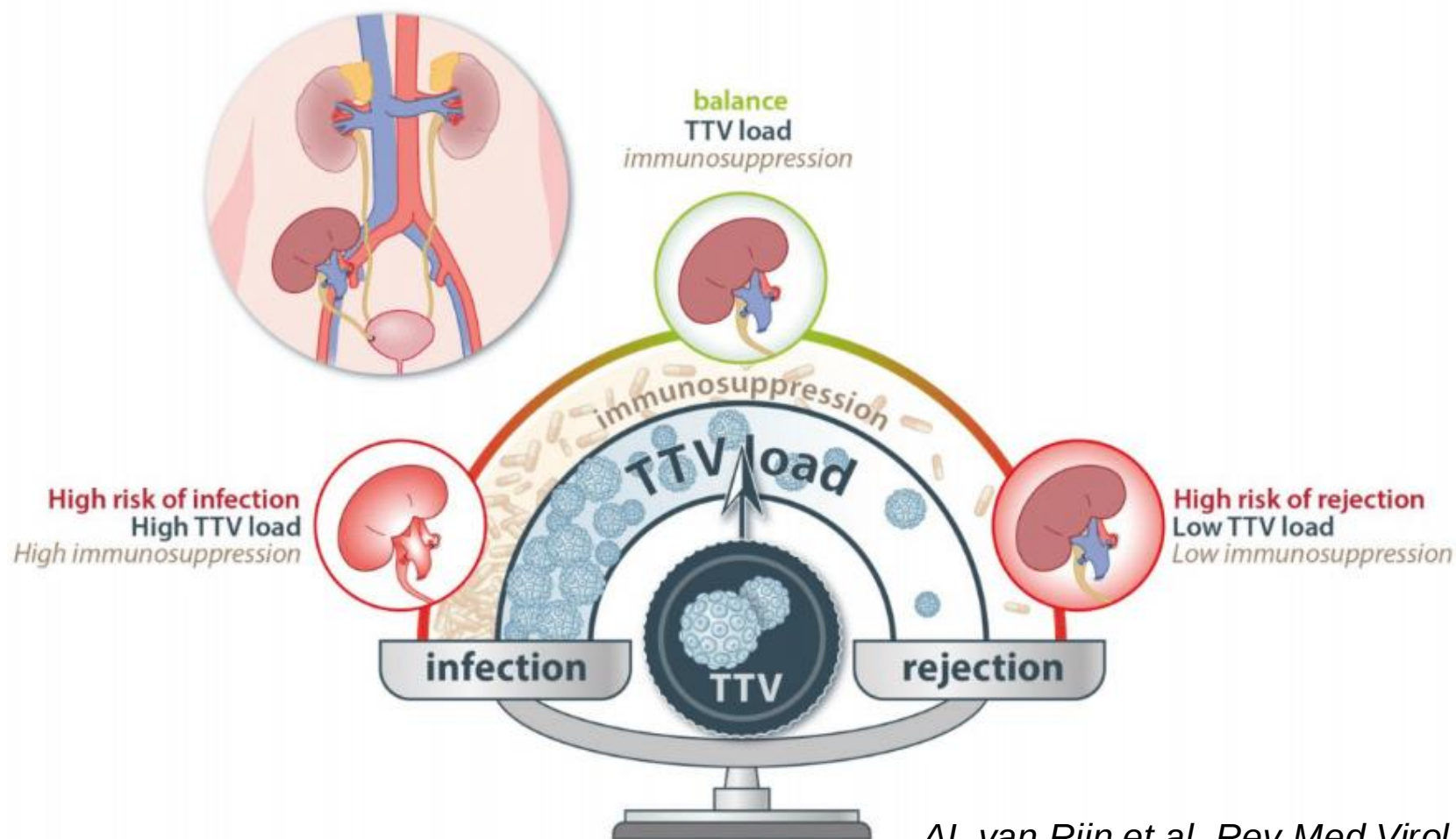


Torque Teno Virus viral load

A biomarker for *immune monitoring* in Solid Organ Transplantation



INTRODUCTION



AL van Rijn et al. Rev Med Virol. 2023



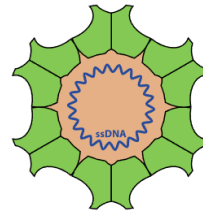
Targetting TTV

What is the good threshold?



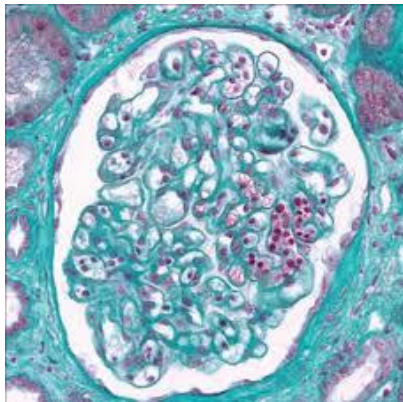
INTRODUCTION

TTV GUIDE ; Bond et al, 2021
KTR < 1 an: **4,2-6,4 log₁₀ cp/mL**

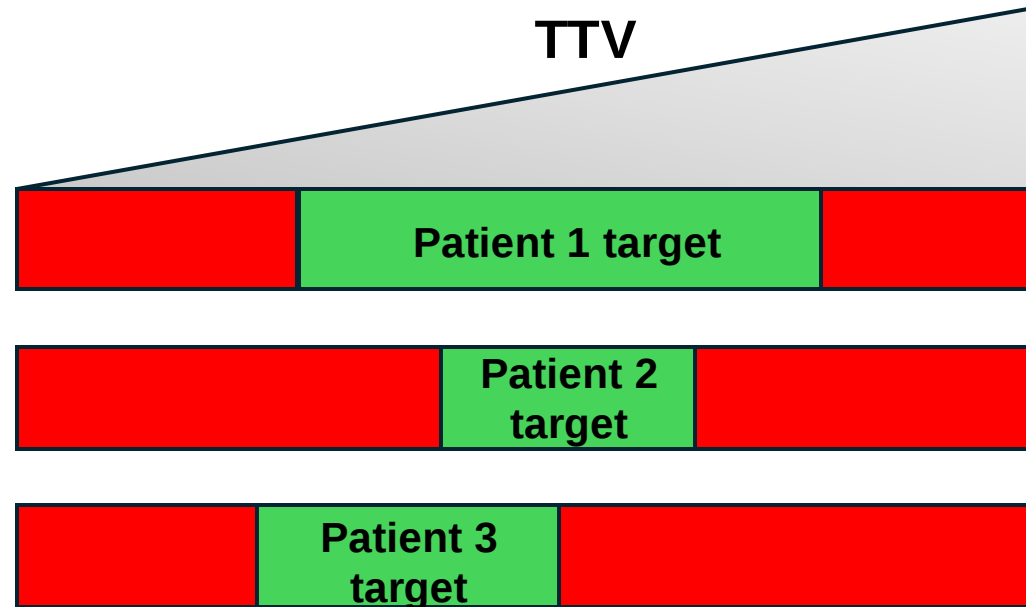


TTV

TAOIST Thaunat, Chauvelot et al. J Med Virol. 2024
KTR > 1 an; **3,75-5,1 log₁₀ cp/mL**



REJECTION



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&
INFECTION

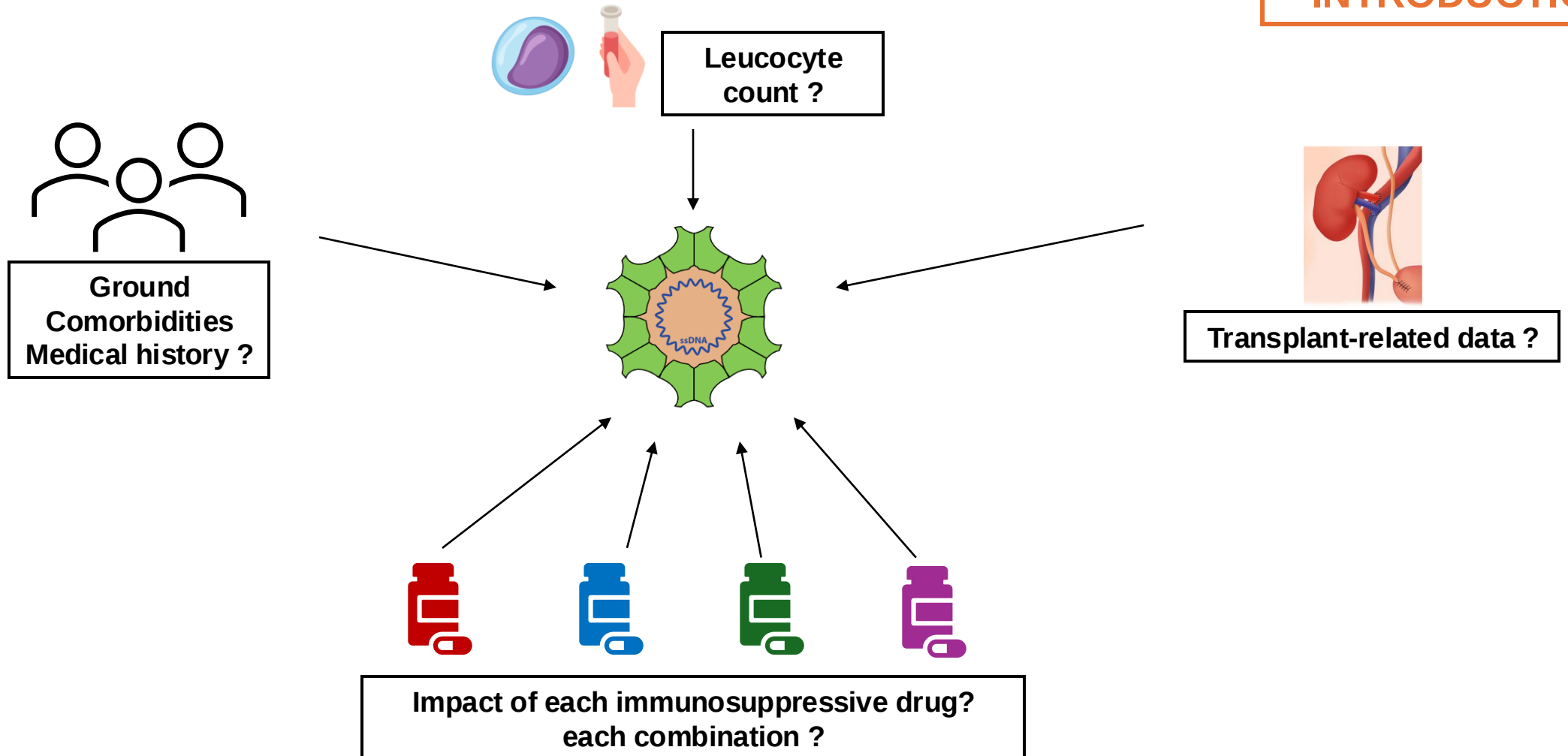


AIM OF THE STUDY

*Describe the **risk factors** influencing TTV load*



INTRODUCTION



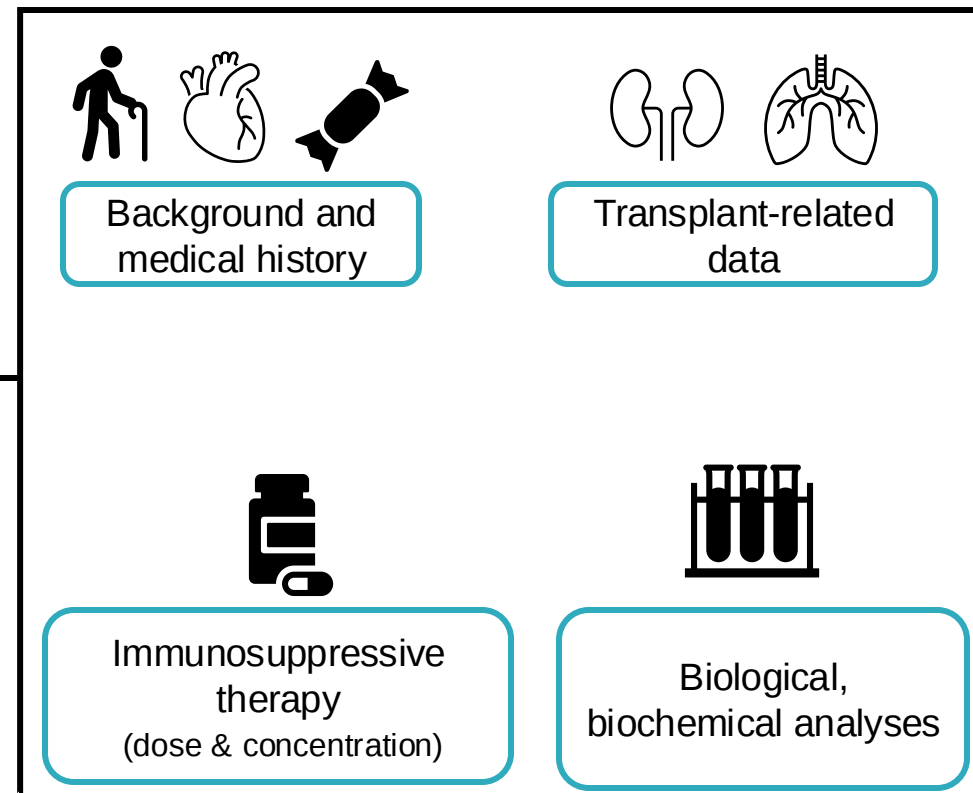
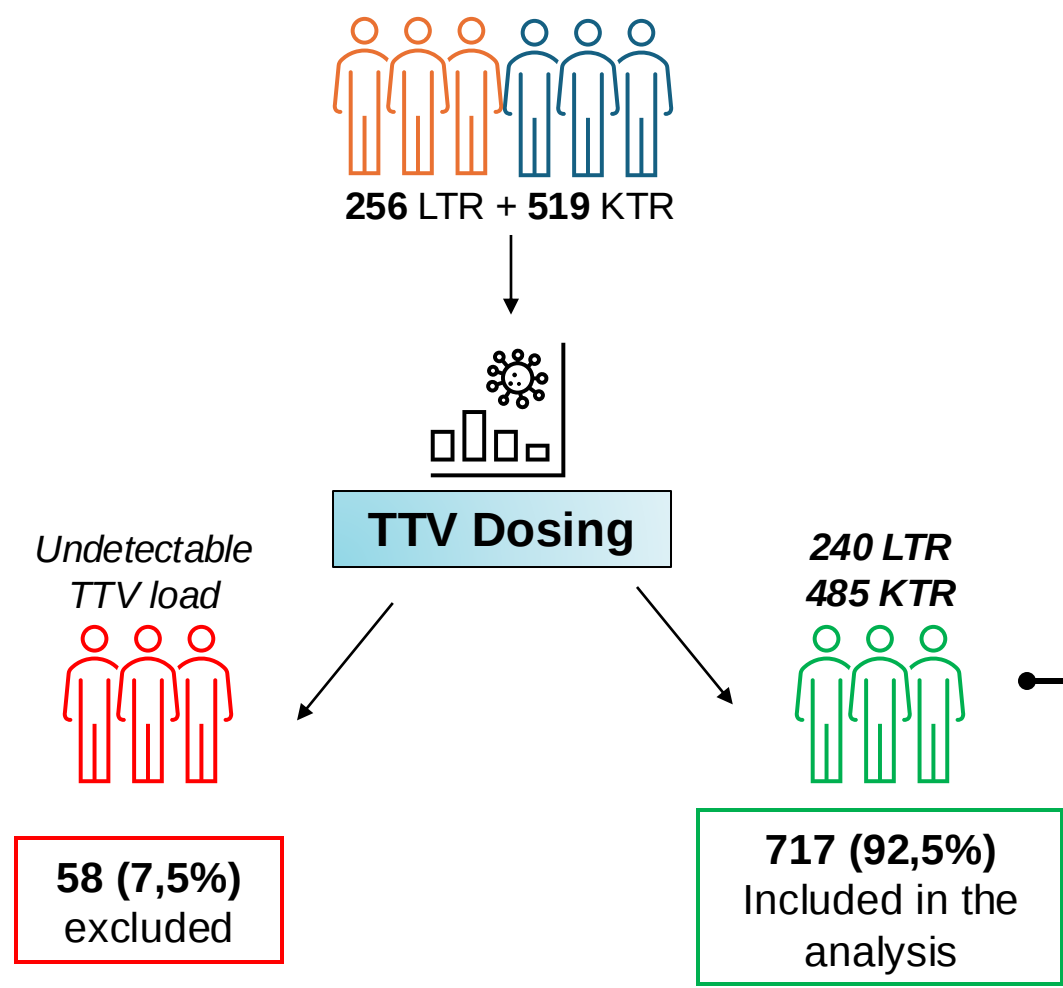


Population:

Transplantation between 1984 et 2021
Cross-sectional, retrospective, monocenter study



METHODOLOGY





Patient characteristics



RESULTATS



CNI

Tacrolimus: n= 508 (71%)

Ciclosporine n = 149 (21%)



Antimétabolites

MMF n = 582 (81%)



Anti-mTor

n=102 (14,6%)



Bélatacept

n=30 (4,2%)



Corticoïdes

n=543 (76%)



62% of mens

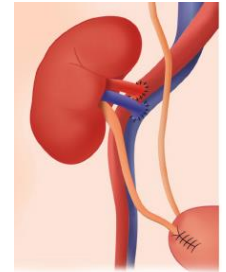
56,7 (13,1) years

IMC: **26,2 (5,7) kg/m²**



Post-Transplant time

6.78 ± 6.75 years



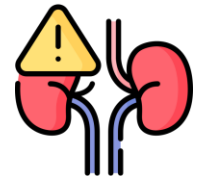
**21% of 2nd transplant
for KTR**



88%



49%

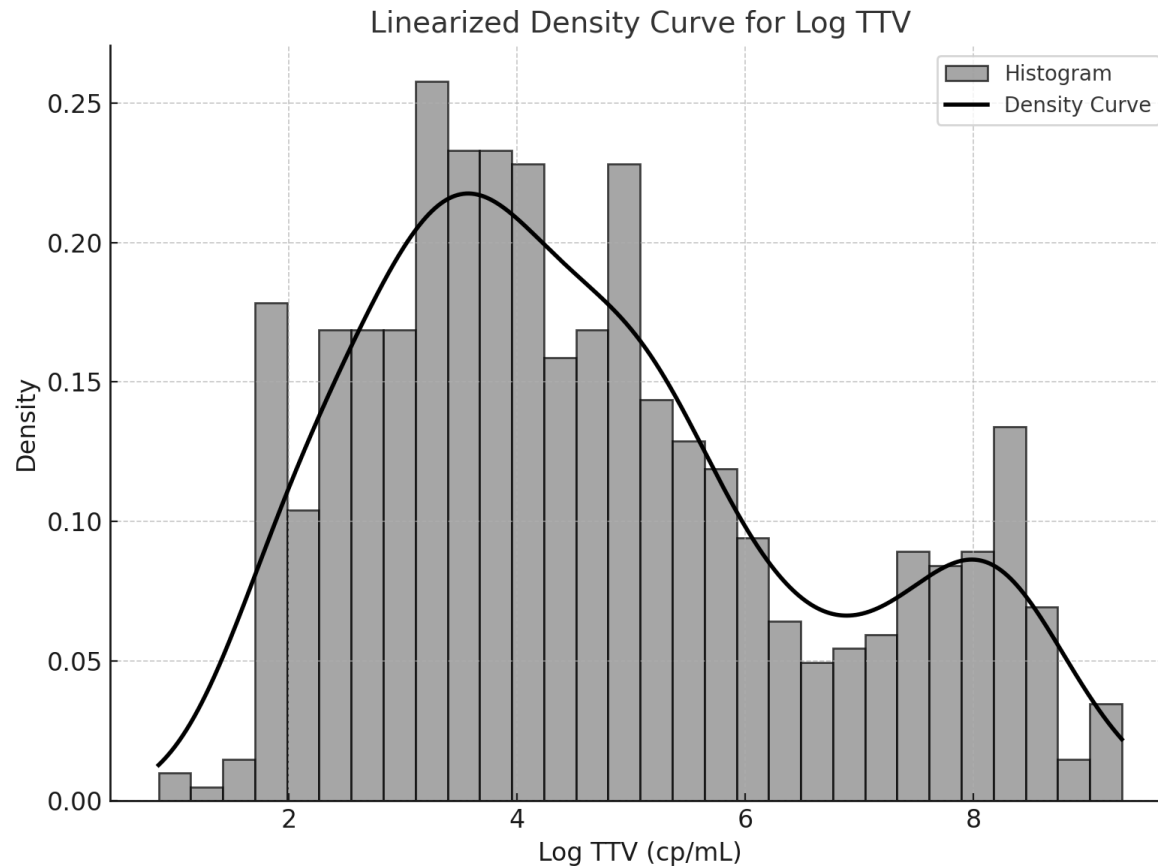


eGFR :

55,6 ± 24,1 ml/kg/1,73m²



TTV viral load distribution

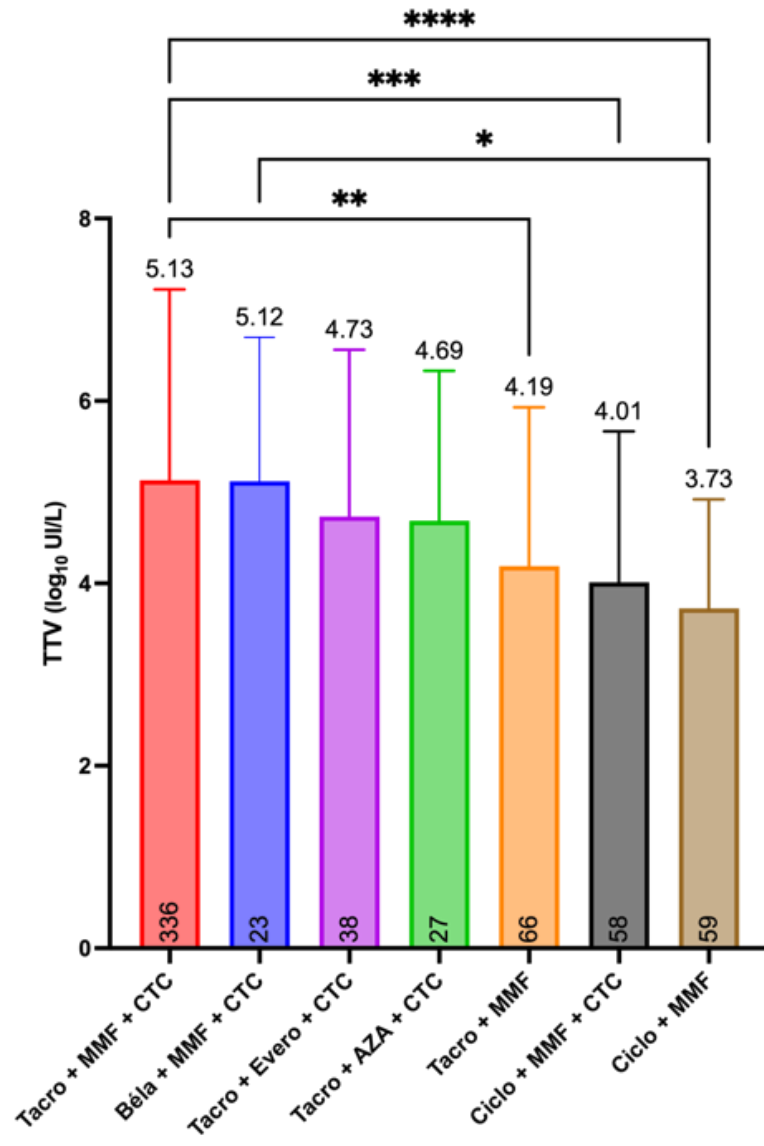


Mean (SD): **4.64 (1.94)** $\log_{10}$ cp/ml

Median [Q25–Q75]: **4.26 [3.17; 5.75]** $\log_{10}$ cp/ml



Combination of Immunosuppressive therapies



Multivariate analysis:

Ciclosporine: **-0,74 (0,18) log₁₀ cp/ml** (p=0,0001)

Steroids: **+0,59 (0,25) log₁₀ cp/ml** (p=0,0198)

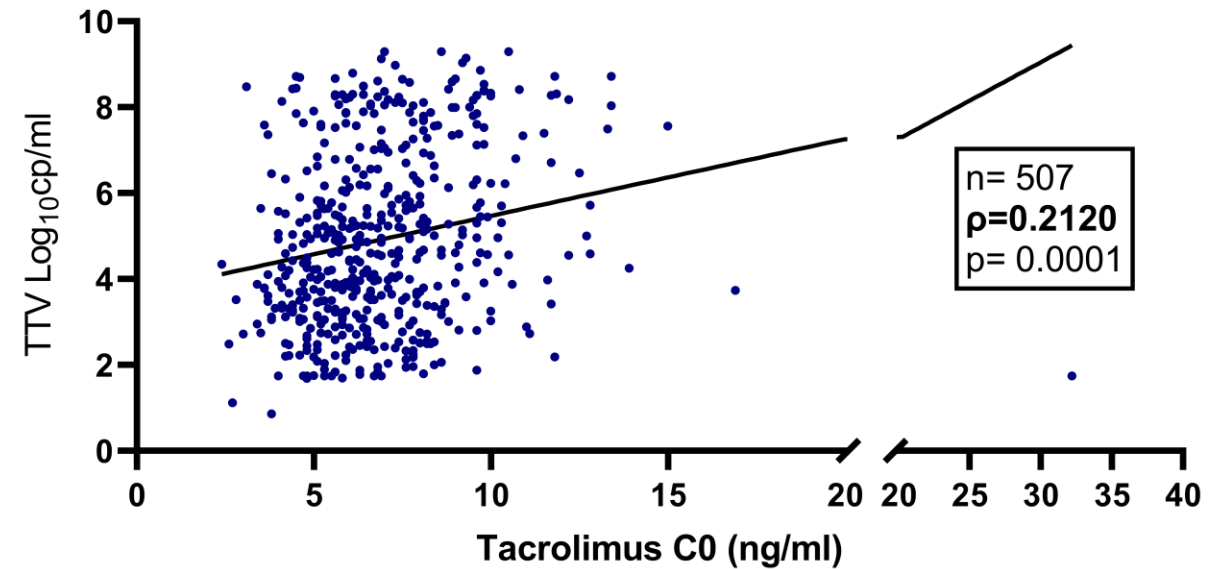
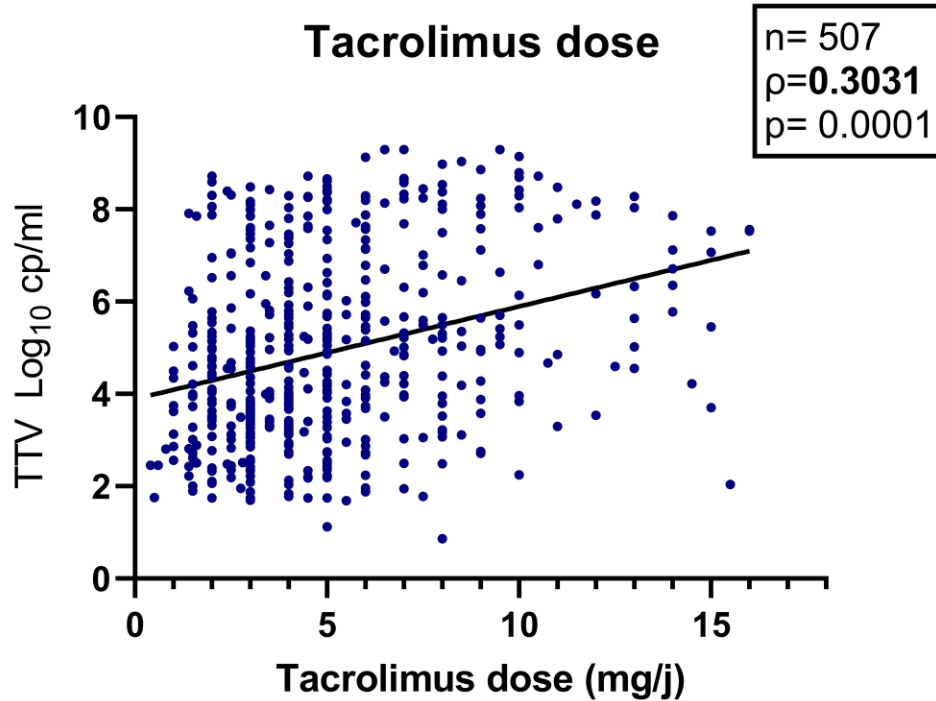
Anti-mTor: not significant

No CNI: not significant

Belatacept: not significant



Tacrolimus (Dose & C0): *mild to moderate correlation*



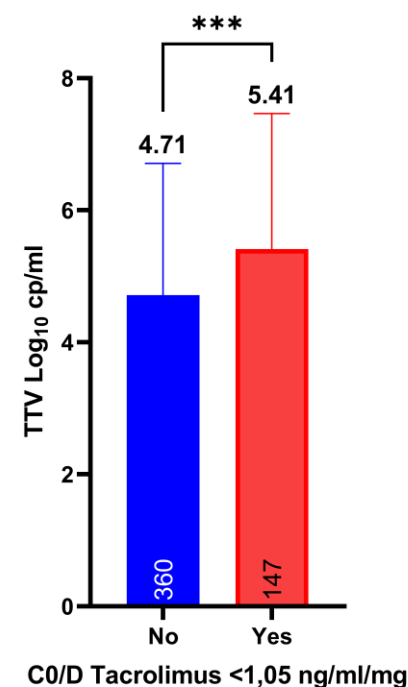
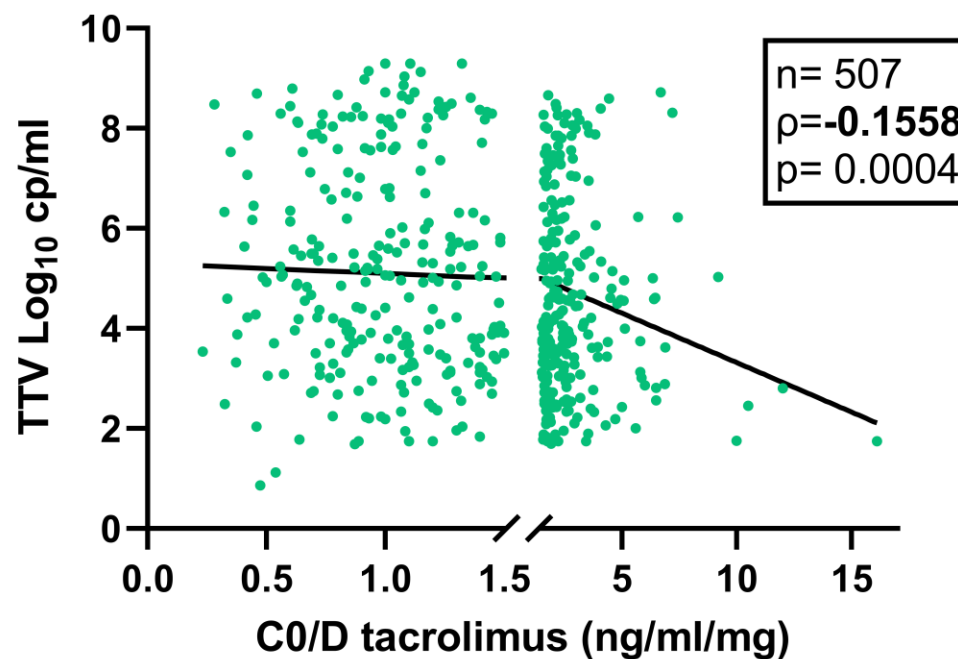
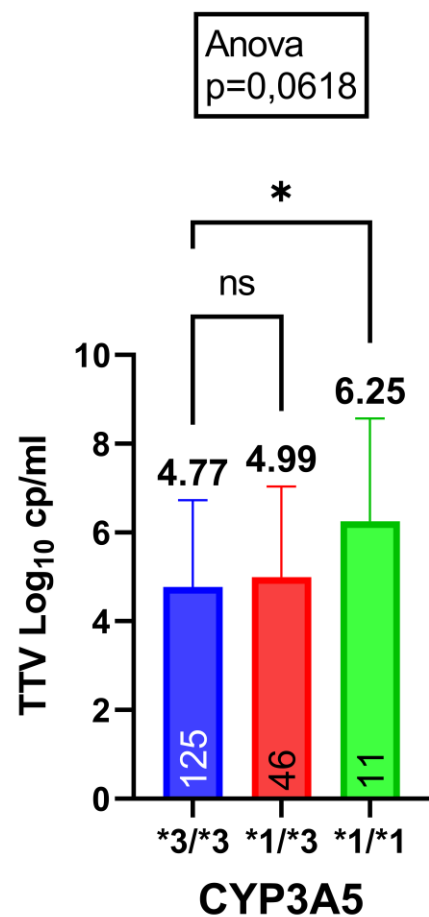
Multivariate analysis:

Tacrolimus Dose: **+0,13 (0,03) log₁₀ cp/ml for each mg/j** (p<0,0001)

C0 Tacrolimus: **+0,15 (0,04) log₁₀ cp/ml for each ng/ml** (p=0,0008)



Metabolism of Tacrolimus



Multivariate analysis:
+0,42 (0,19) log₁₀ cp/ml if C0/D < 1,05 ng/ml/mg ($p=0,0268$)

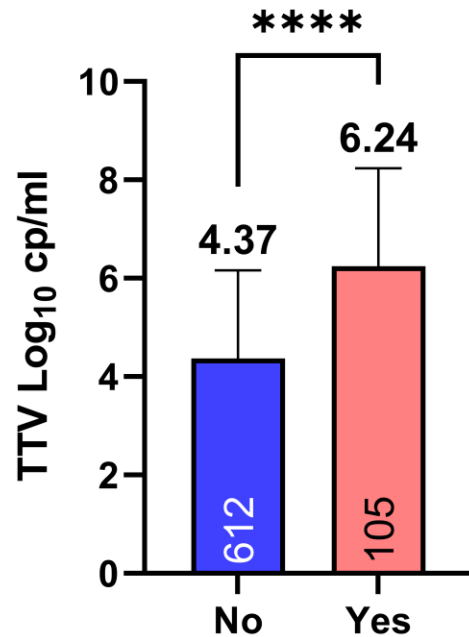


Induction & Rituximab therapies



RESULTATS

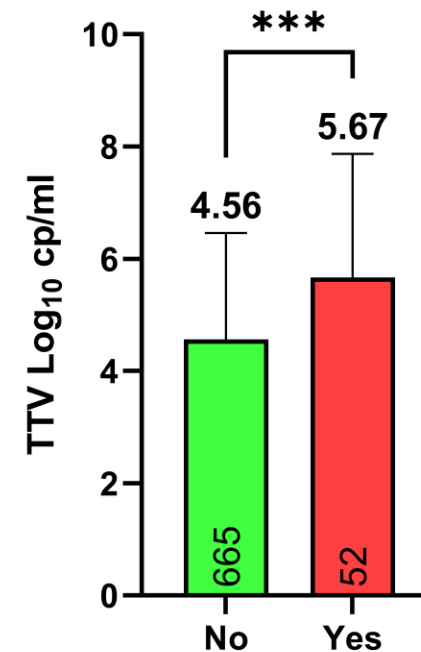
Median Time to TTV assay: 30 months



Induction treatment within the year of dosing

Multivariate analysis:

-1,82 (0,24) log₁₀ cp/ml if no induction within the year (p<0,0001)



Rituximab without any delay

Multivariate analysis:

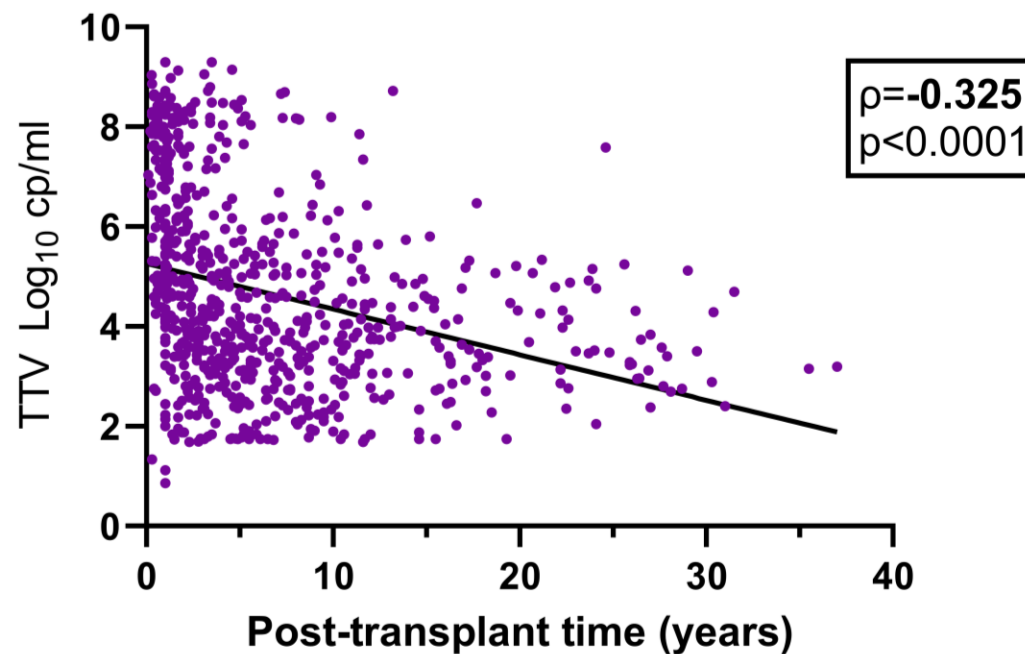
0,97(0,27) log₁₀ cp/ml with RTX infusion (p=0,0004)



Post-Transplant Time



an average Post-Transplant Time of 6.78 ± 6.75 years



Multivariate analysis:

-0,04 (0,01) $\log_{10}$ cp/ml for each year after transplantation ($p=0,0013$)



Patient Background



$r = -0,075$ $p = 0,035$

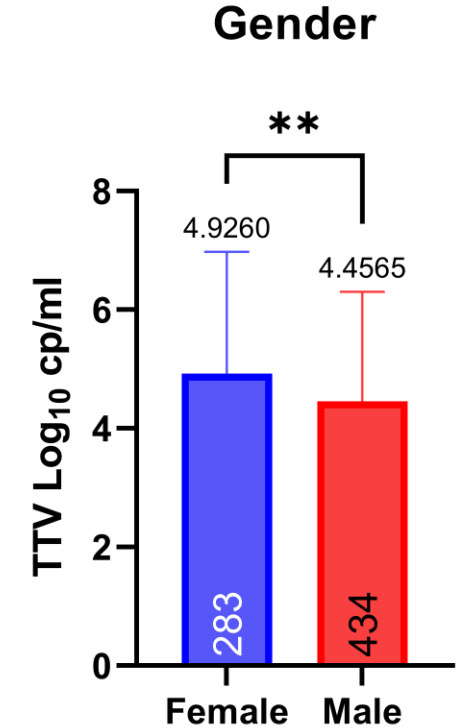
Multivariate analysis:
Not significant



$r = -0,08$ $p = 0,035$



Multivariate analysis:
+0,35 (0,14) $\log_{10}$ cp/ml
with female gender ($p = 0,0119$)

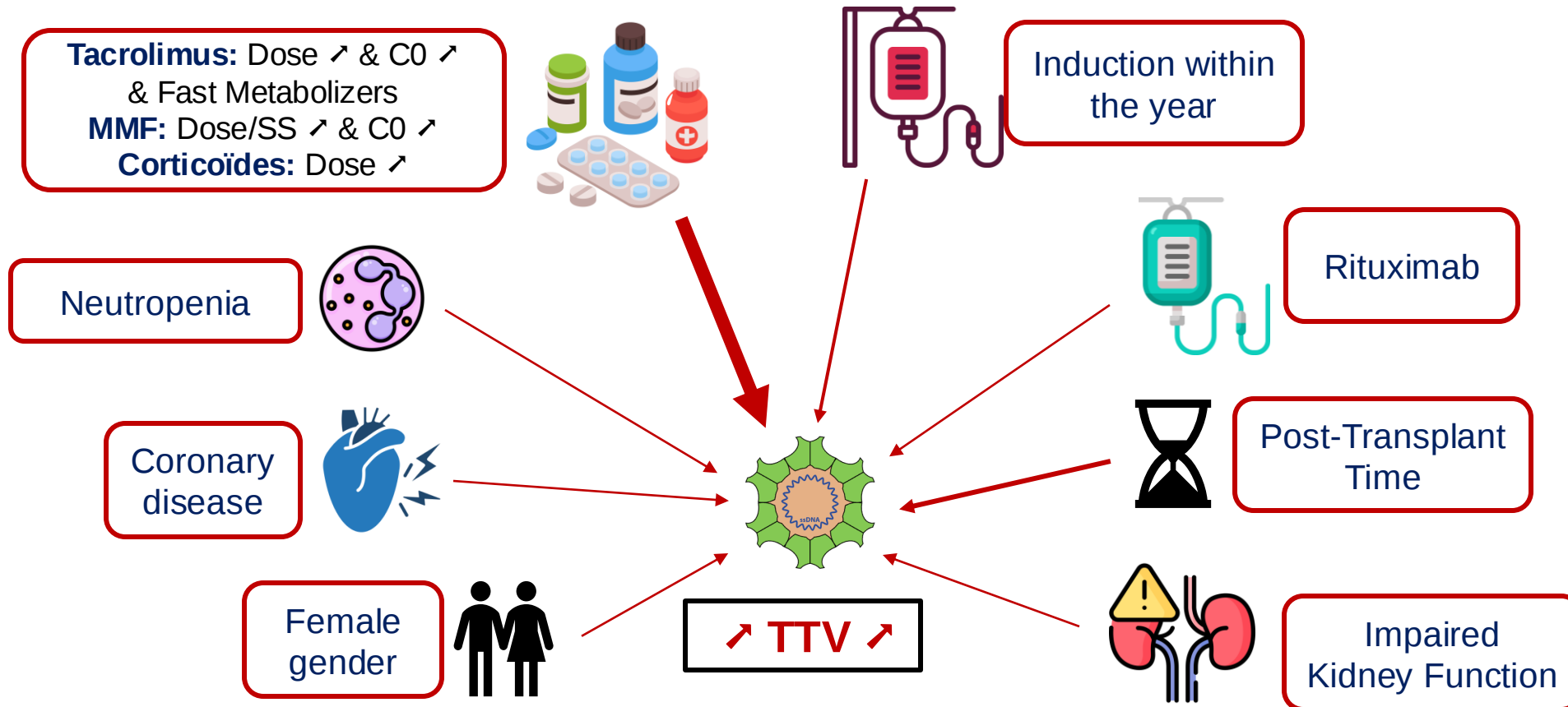




Factors of TTV viral load: *Immunosuppressive treatment weight*



717 KTR + LTR with an average Post-Transplant Time of 6.78 ± 6.75 years





TTV GUIDE

Torque Teno Virus
Based Immune Monitoring



UNIVERSITÉ DE STRASBOURG



VIRUS ET GREFFES 2025

ACKNOWLEDGEMENT

Virology Department

Pr Samira FAFI-KREMER

Dr Morgane SOLIS

Dr Floriane GALLAIS

Nephrology Department

Dr Ilies BENOTMANE

Pr Sophie CAILLARD-OHLMANN

Pr Bruno MOULIN

Pneumology Department

Dr Benjamin RENAUD-PICARD

Pr Romain KESSLER

And

Dr Estelle AYME-DIETRICH

Dr Fanny REYSZ,

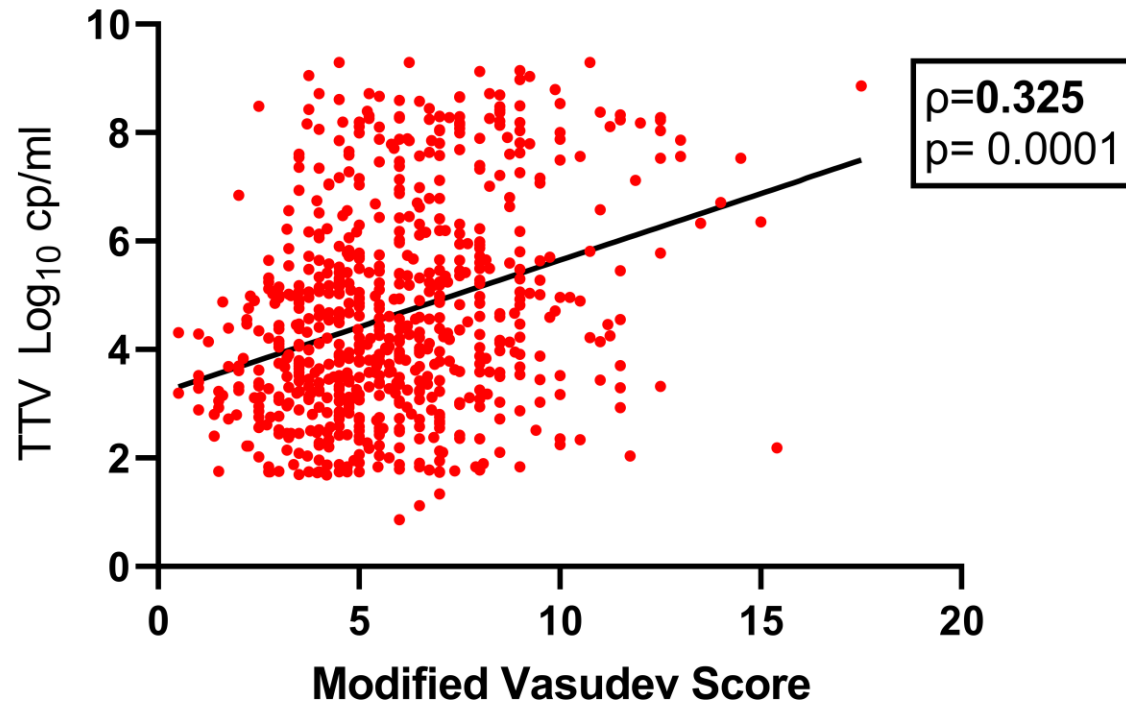
Dr Joris MULLER

Sophie-Jaeger, François Bischoff, Danielle Roy





Modified Vasudev score

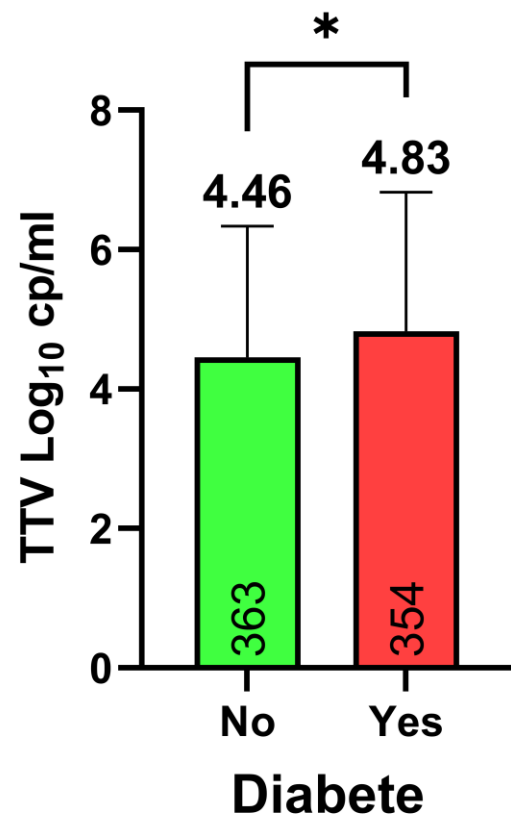


Immunosuppressant	Dosage	Points
Tacrolimus	2 mg	1
Cyclosporine	100 mg	1
Belatacept	N/A	5
Mycophenolate mofetil / Myfortic	500 mg	1
Leflunomide	10 mg	1
Azathioprine	100 mg	1
mTOR inhibitors (e.g., Sirolimus, Everolimus)	2 mg	1
Corticosteroids	5 mg	1

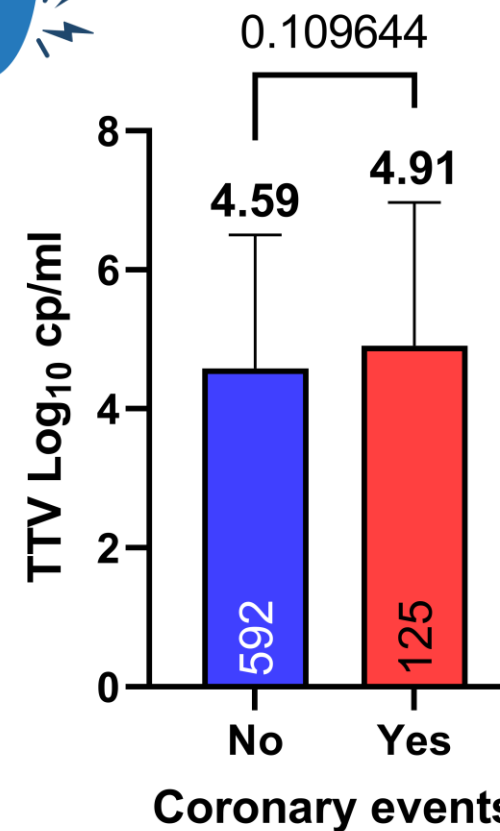
Multivariate analysis:
+0,19 (0,05) log₁₀ cp/ml for each point ($p=0,0002$)



Comorbidities: cardiovascular history



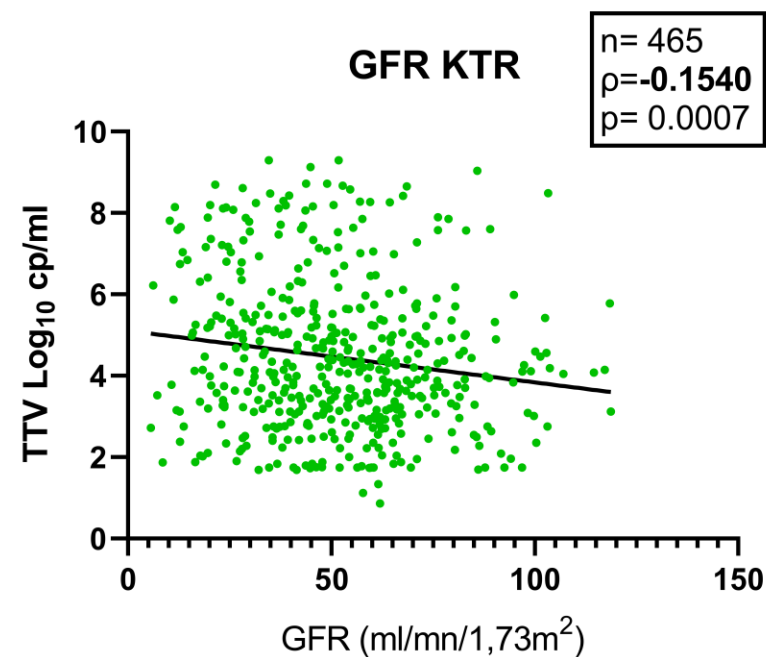
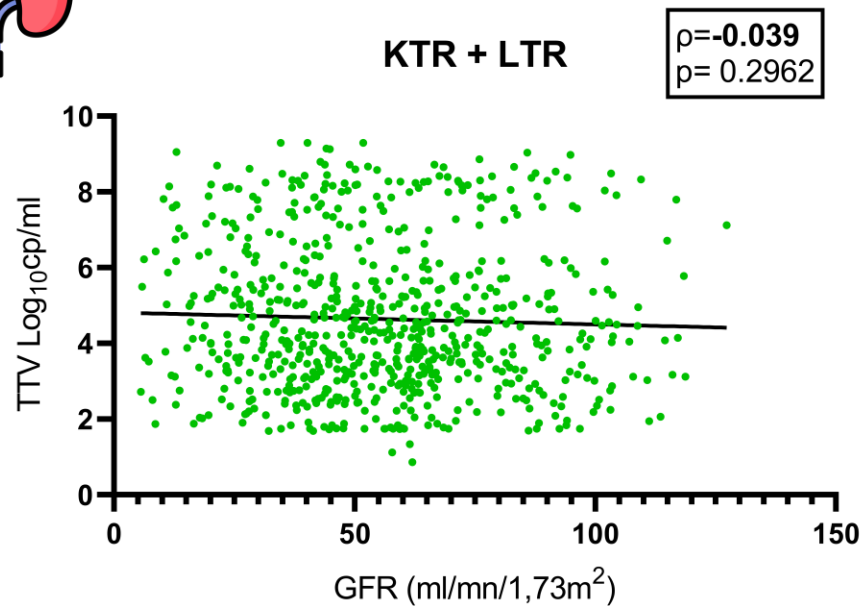
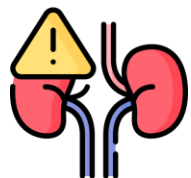
Multivariate analysis:
Not significant



Multivariate analysis:
+0,58 (0,24) log₁₀ cp/ml
with coronary event
(p=0,0194)



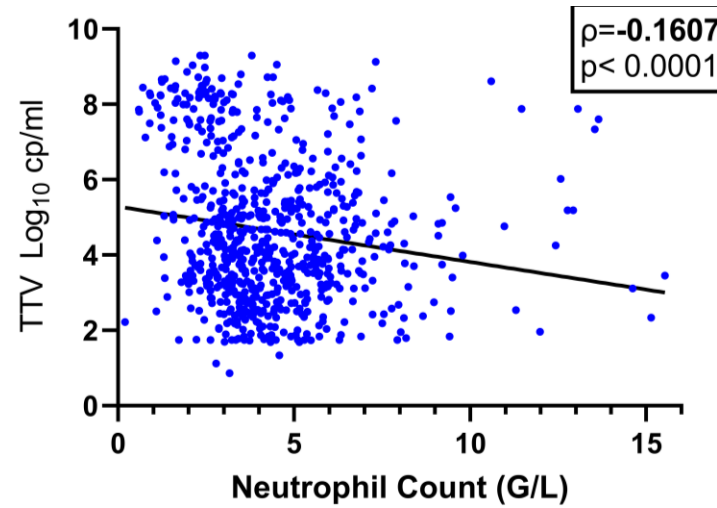
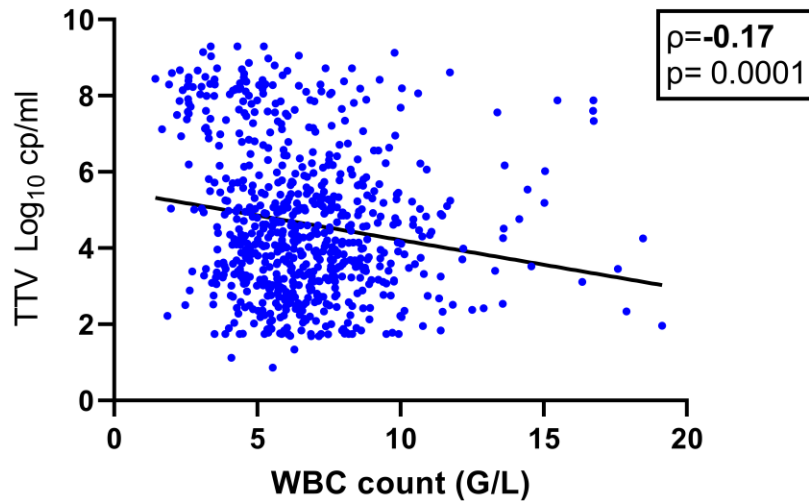
Comorbidities: kidney function



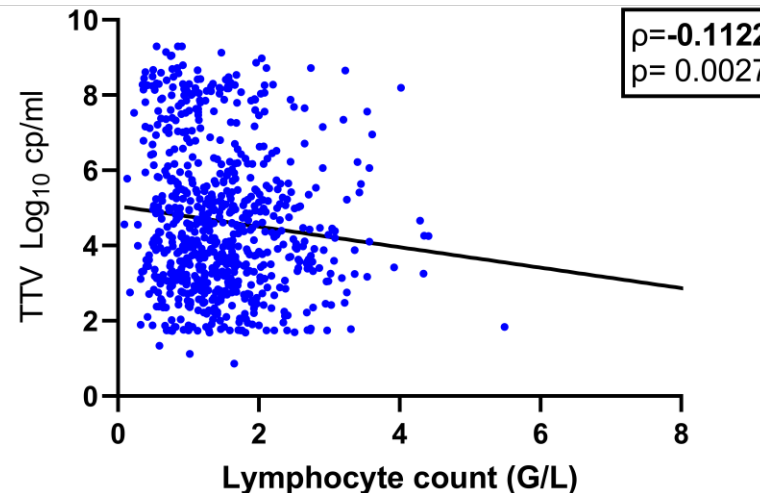
Multivariate analysis:
-0,135 (0,040) log₁₀ cp/ml for each decrease
10ml/mn/1,73m² in GFR ($p=0,0009$)



White blood cells: *mild correlation*



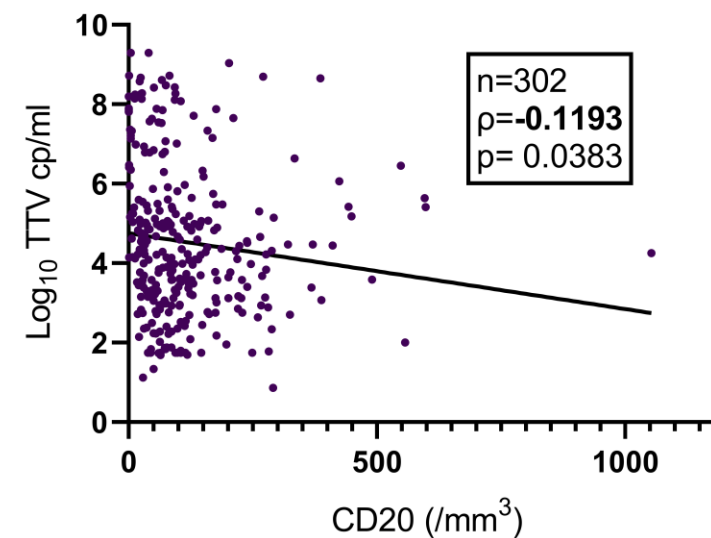
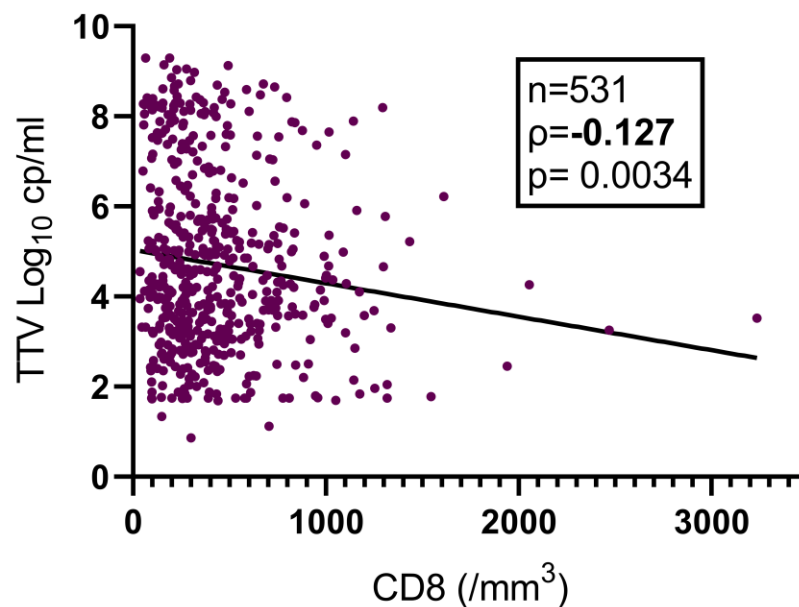
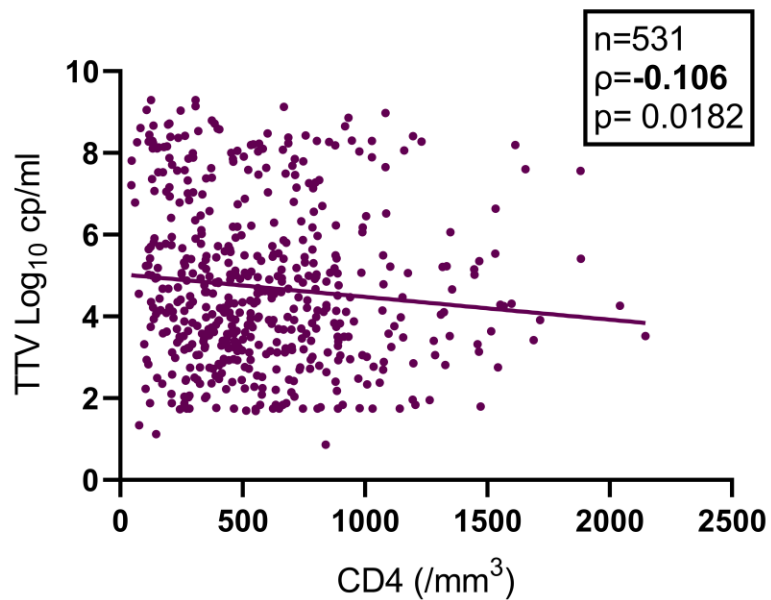
Multivariate analysis:
-0,14 (0,04) log₁₀ cp/ml for each Giga/L decrease in neutrophils ($p=0,0004$)



Multivariate analysis:
Not significant

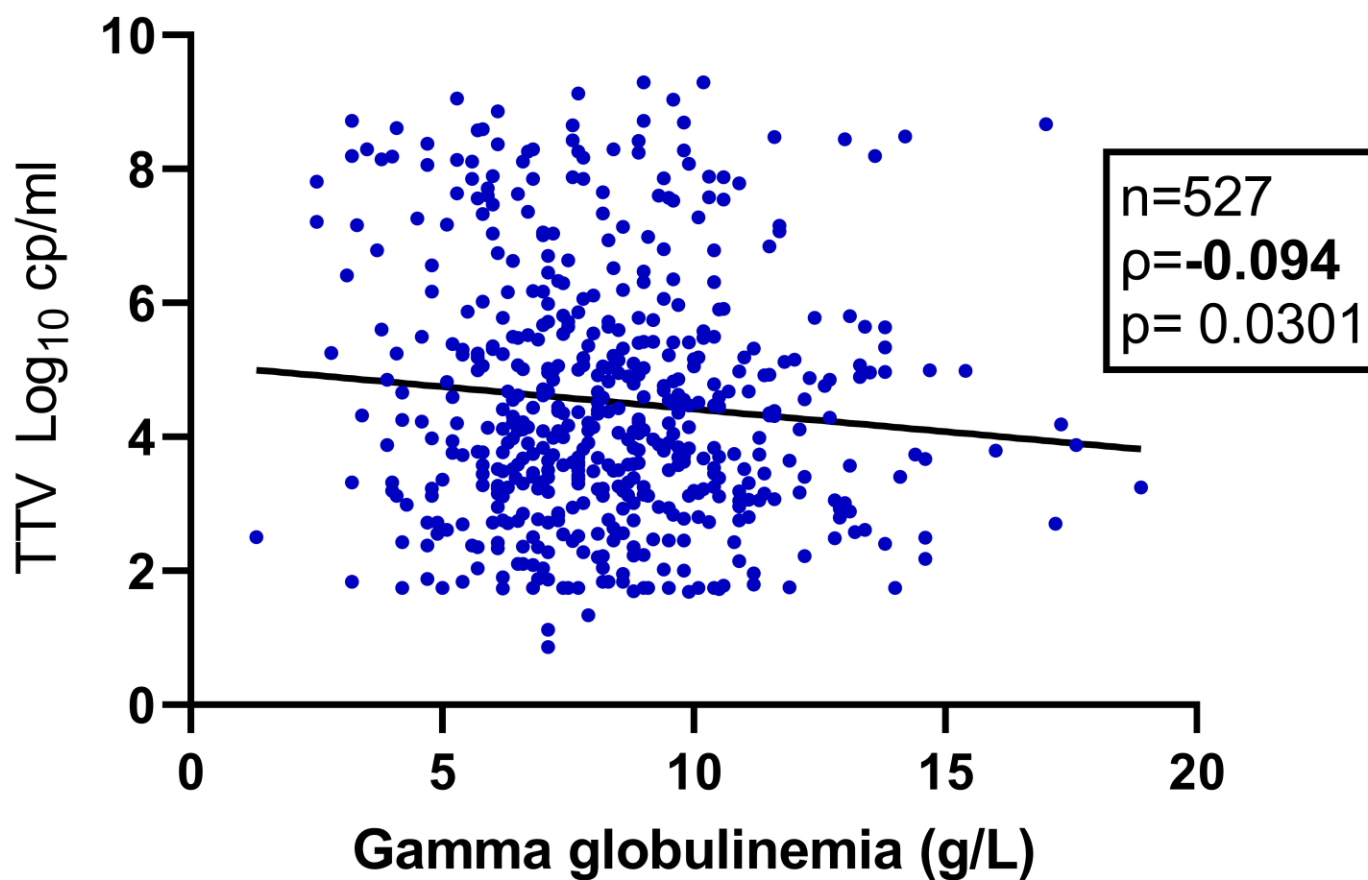


Lymphocyte sub-populations: *mild correlation*





Gammaglobulinemia

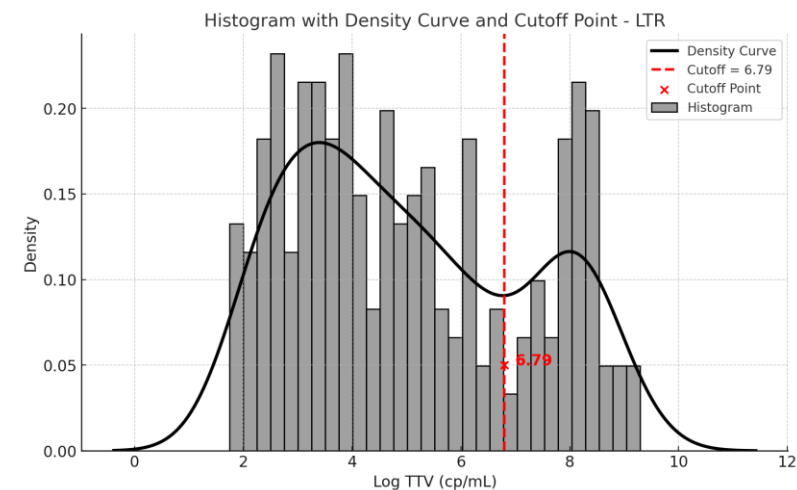
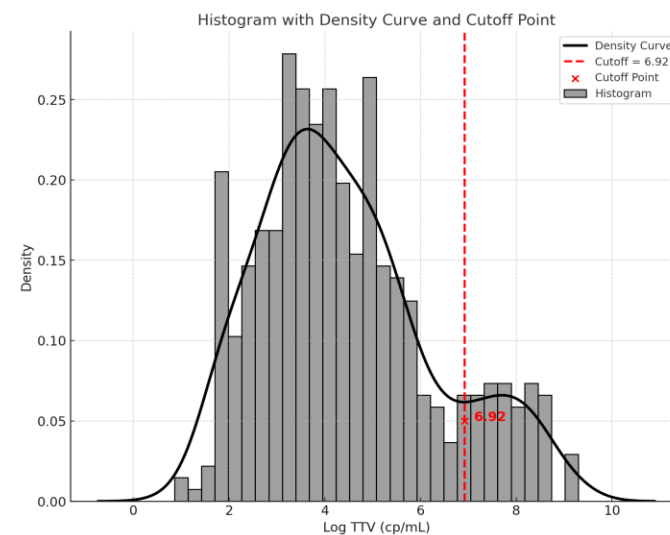
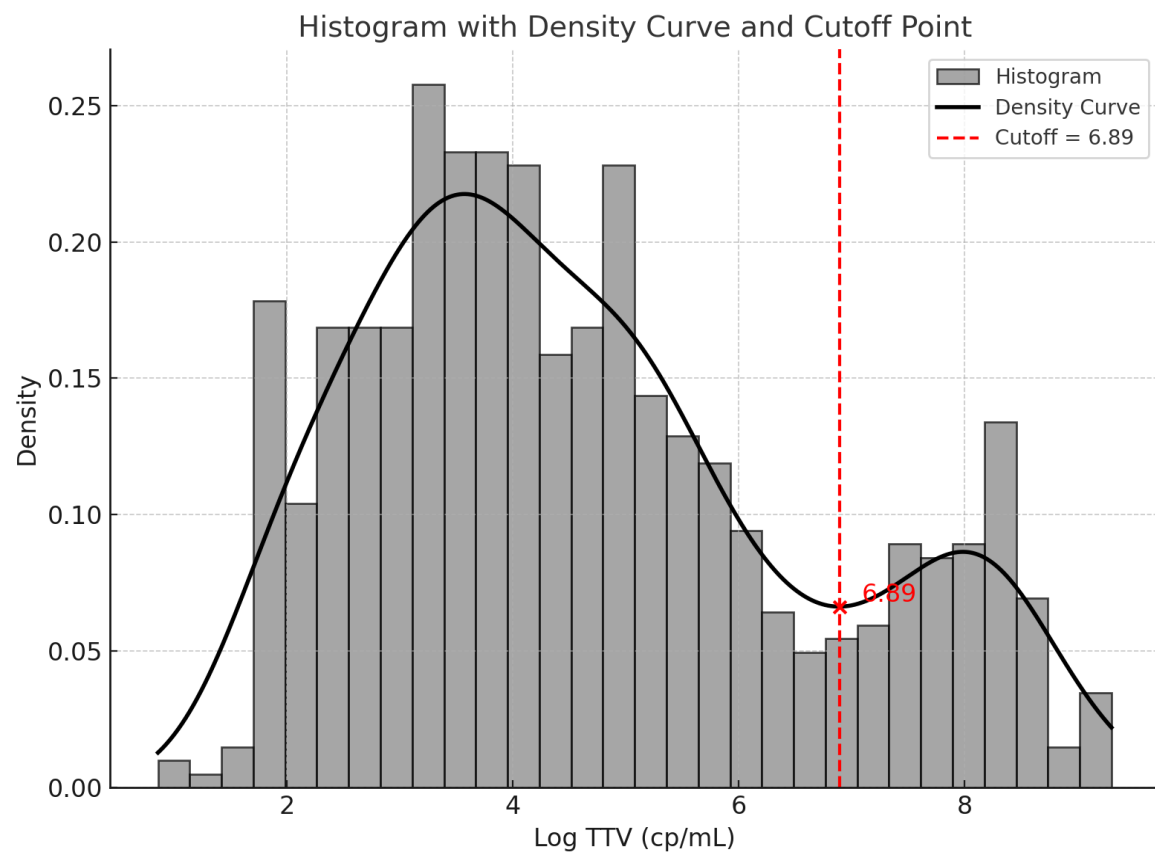




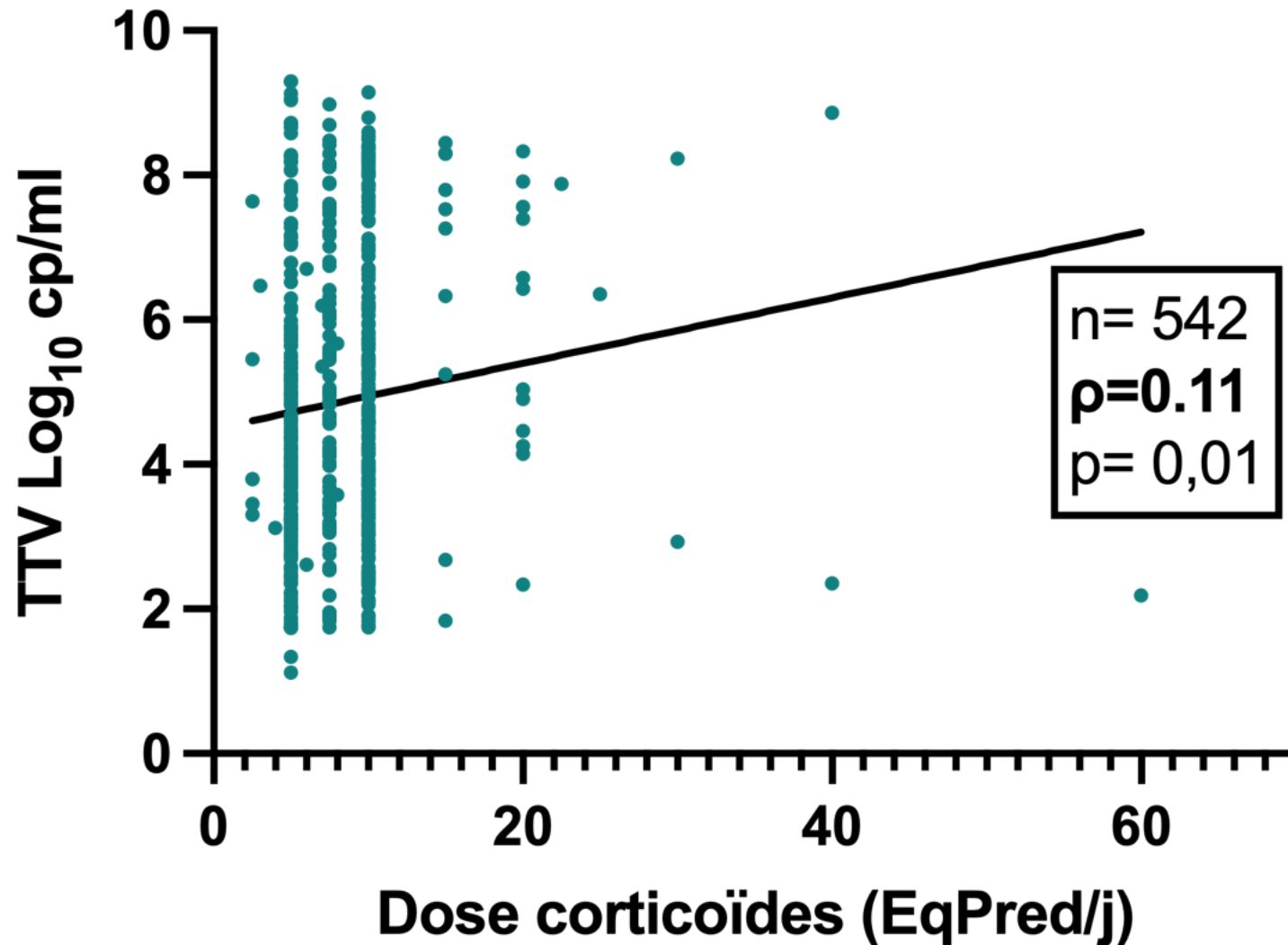
Distribution (complément)



RESULTATS



Impact de la corticothérapie: *corrélation avec la dose*



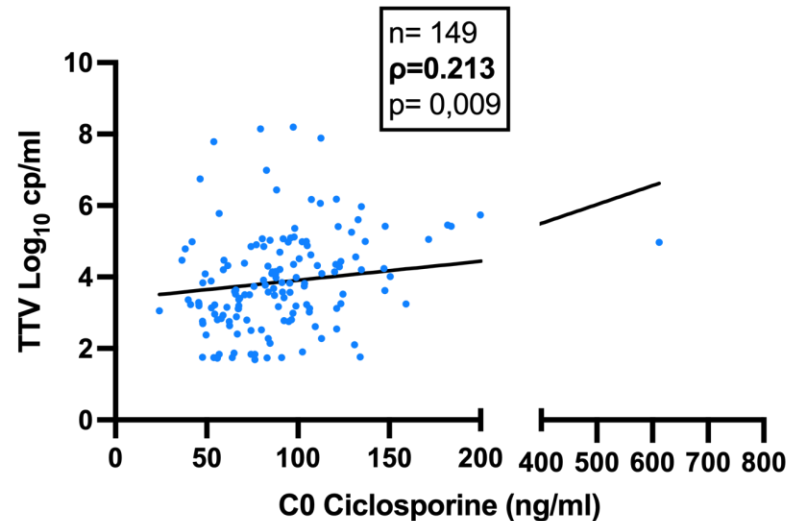
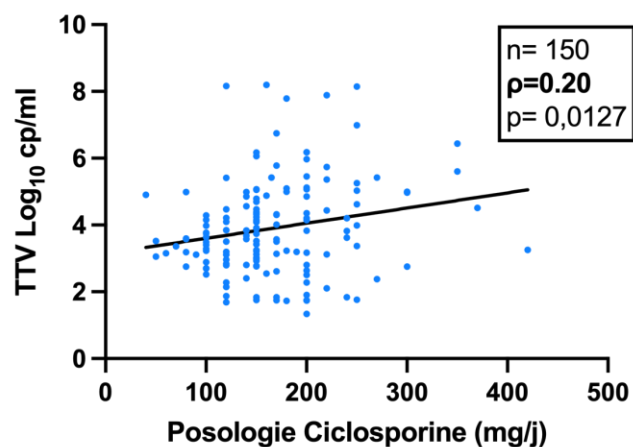
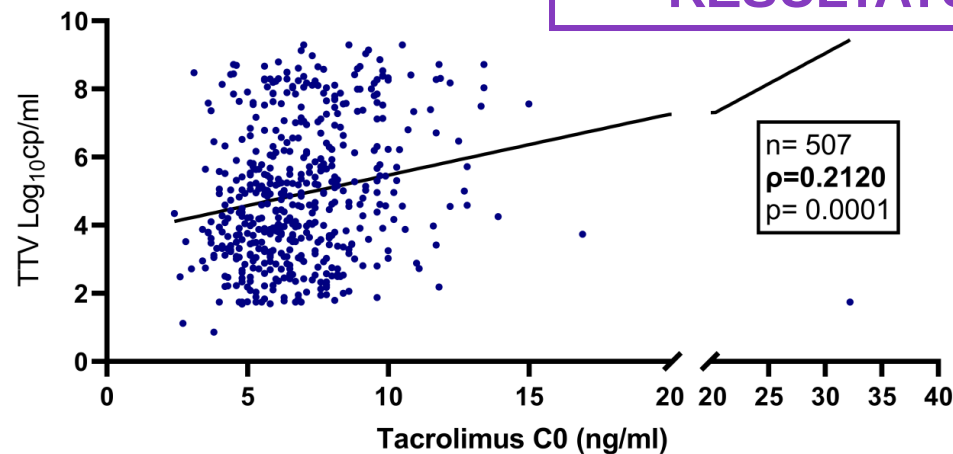
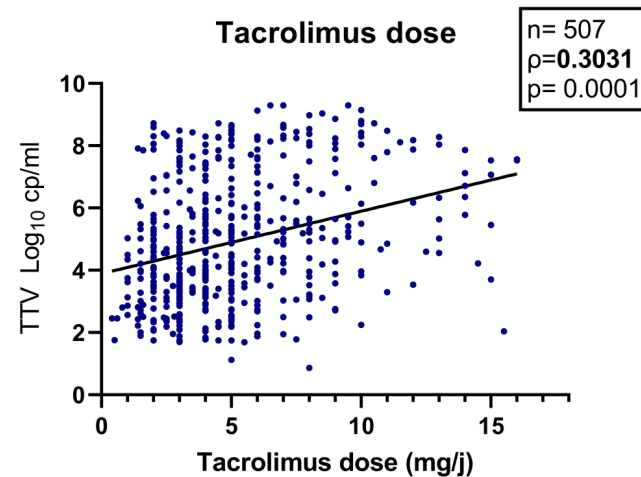
Surveillance thérapeutique pharmacologique *CNI*



Analyse multivariée

Posologie Tacrolimus:
+0,13 (0,03) $\log_{10}$ cp/ml
par mg/j ($p < 0,0001$)

C0 Tacrolimus:
+0,15 (0,04) $\log_{10}$ cp/ml
par ng/ml ($p = 0,0008$)



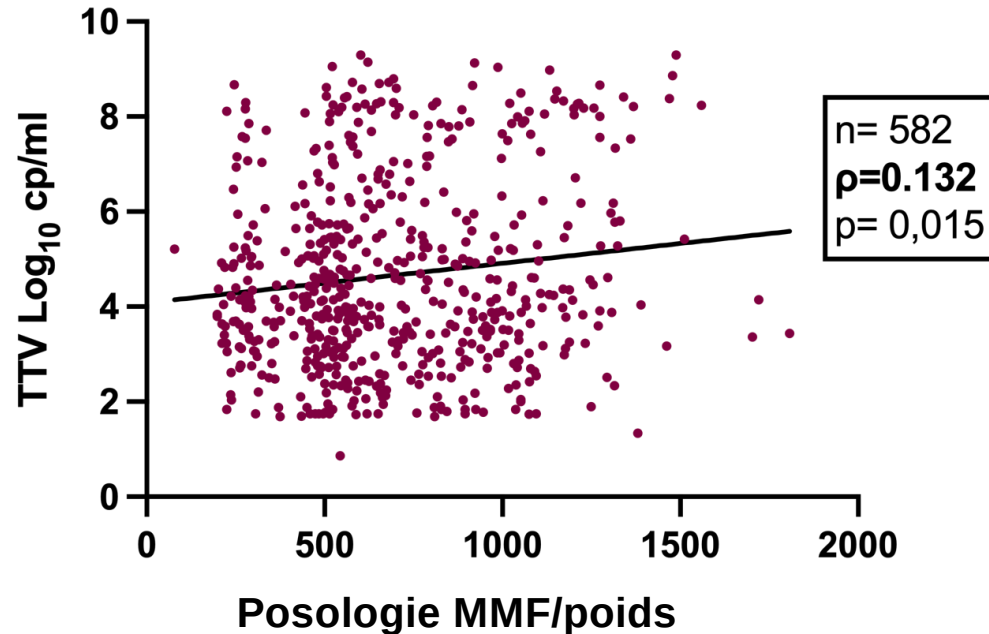
Surveillance thérapeutique pharmacologique *MMF*



Analyse multivariée

+0,30 (0,12) $\log_{10}$ cp/ml par 10mg/kg/j ($p=0,0113$)

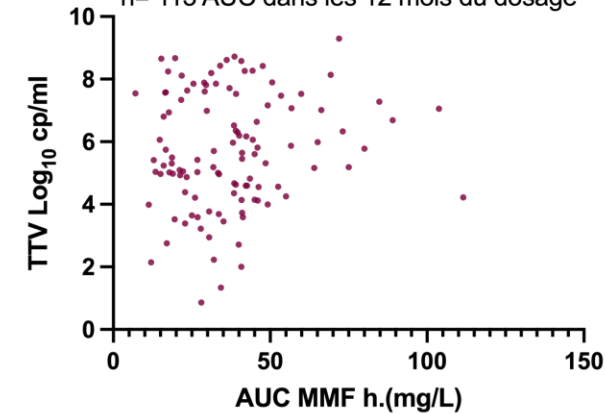
$\rho=0,09$ pour posologie MMF seule
Posologie moyenne 1299 (573) mg/j



Cohorte KTR

Pas de corrélation, $p=0,18$

$n=113$ AUC dans les 12 mois du dosage



Cohorte LTR

