



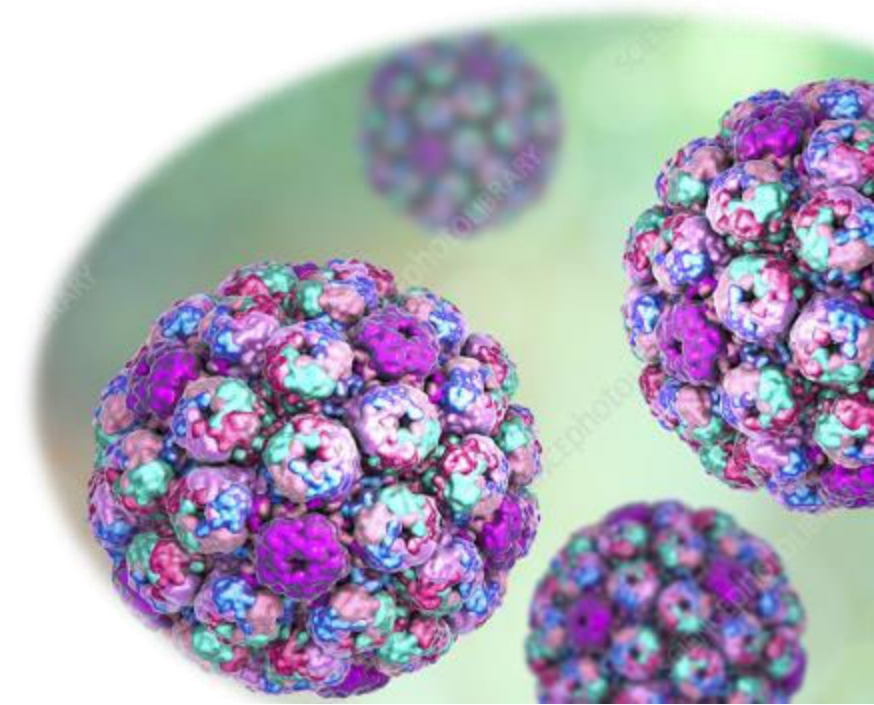
Torque teno virus load and antiviral T-cell immune response after belatacept initiation in kidney transplant recipients

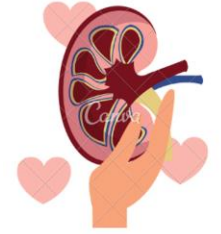
Dr TRUFFOT Aurélie

PHU, laboratoire de virologie

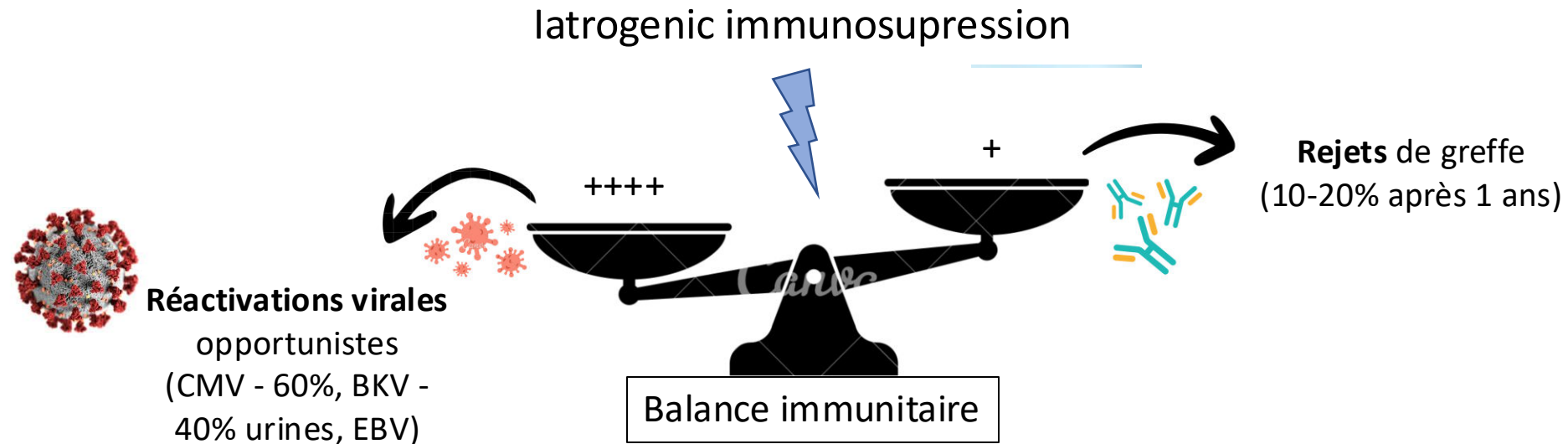
CHU Grenoble Alpes

Le 13 Janvier 2024





Follow-up for kidney transplant recipient



- Therapeutic pharmacological monitoring
- qPCR – opportunistic viral load monitoring
- CMV serology

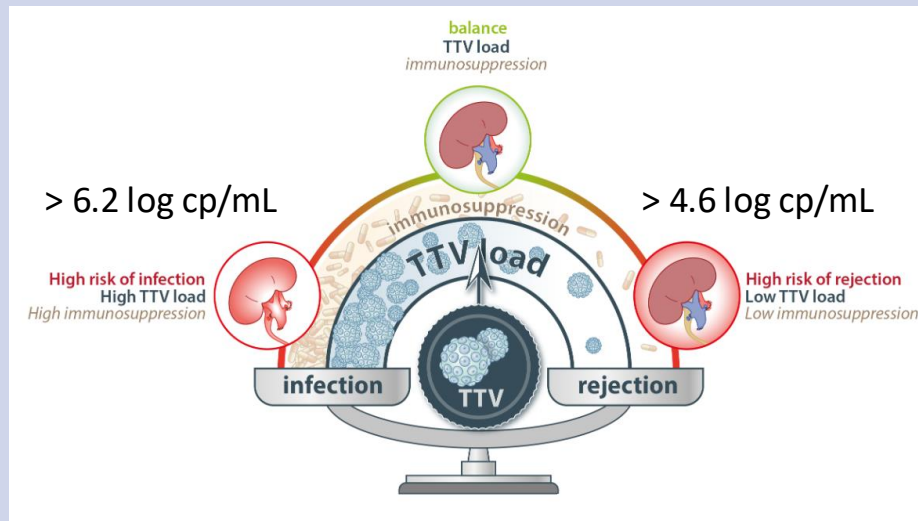
Not enough

Need to find new biomarkers to help clinician's monitoring and to assess the immune status

Context

Virological tools

Torque Teno Virus (TTV) :
a new biomarker to predict infections and
graft rejection ?



Rijn et al. – Haupenthal et al. 2023. TTV Guide

Immuno-virological tools

Anti-viral Cell Mediated Immunity (CMI)
IFN- γ Release Assay = IGRA

	Matrix	Activation 37°C	Revelation
QuantiFERON®	Whole blood	16h	ELISA
VIDAS®-IGRA	Whole blood	16h	ELFA
ELISpot-T IFN- γ	PBMC	24h	Spot/colorimetry

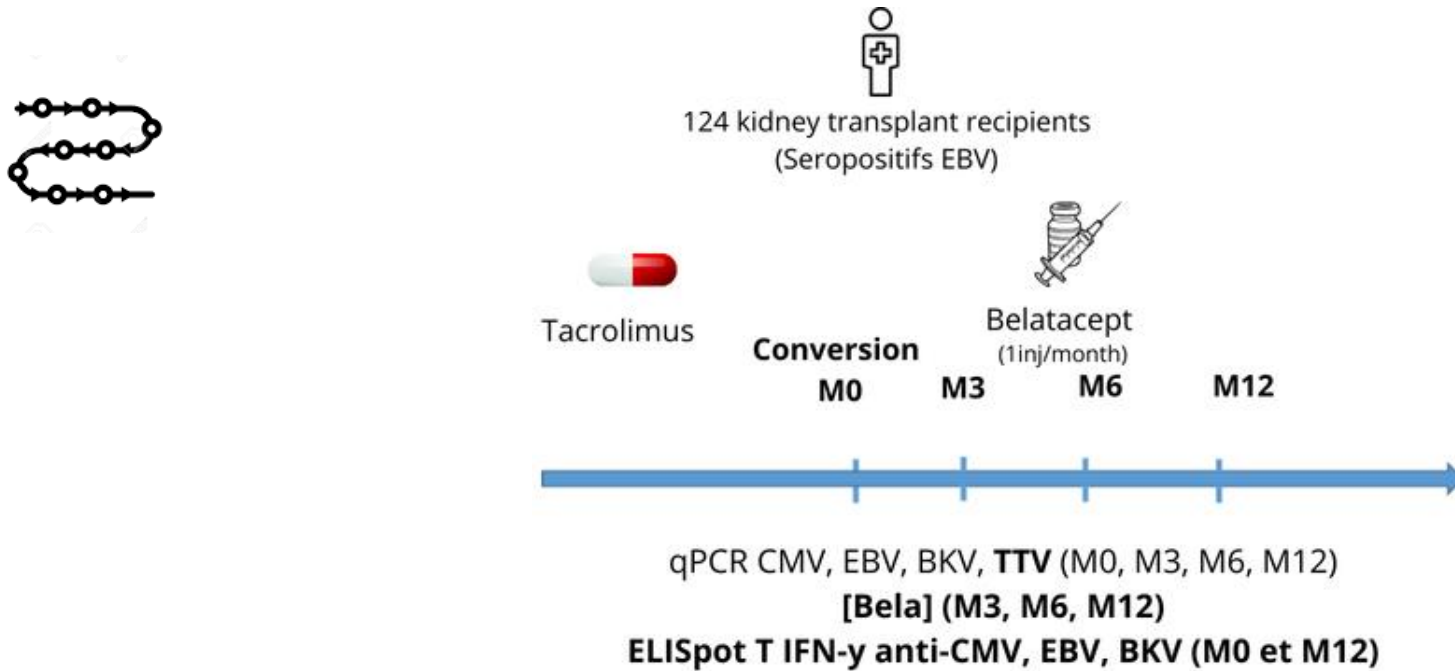
Need standardization

Prakash et al. – Blom et al. – Bestard et al.



Evaluated in tacrolimus treated recipients → **Impact of a tacrolimus-to-belatacept conversion on the TTV load and CMI response**

Material & Method



To date, only 97 recipients underwent the M12 visit (116 recipients for M6)
→ inclusions still ongoing



62 %



59
years old



4 years
between
graft and
belatacept

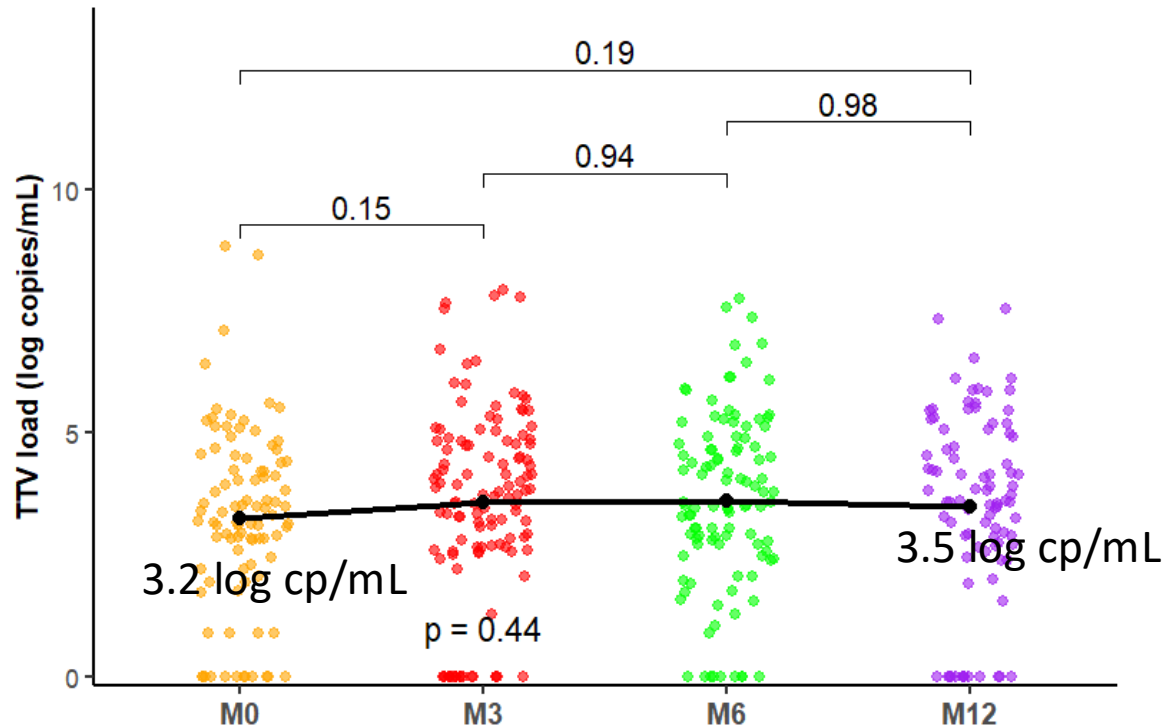
CMV
seropositif

69 %

Opportunistic **viral reactivation**
during th follow-up

CMV : 16 % (n=20)
EBV : 18 % (n=22)
BKV urinary : 35 % (n =44)

Results : impact of belatacept-conversion on TTV load



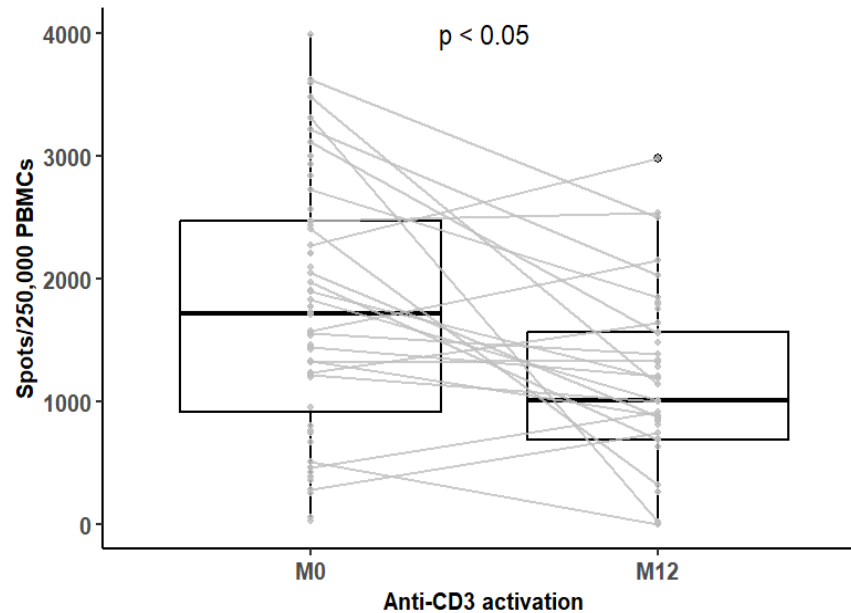
Agreement with 2 other studies :

- Cabezas L., Truffot A. et al. KIR, 2024 (n=68)
- Bredewold, J. Med. Virol, 2024 (n=105)
#negative TTV qPCR were excluded
TTV load M0 = 4.3 log cp/mL
↓
Conversion : 2.2 years post-transplantation

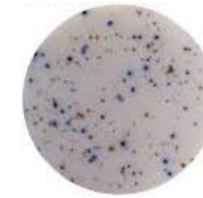
- **No impact** of the conversion to belatacept on TTV DNA load
- Factors influencing : delay between **belatacept-conversion and the transplantation** ($p < 0,05$)
age the day of the conversion ($p < 0,05$)
- No relation between TTV load and belatacept concentration

Results : impact of belatacept-conversion on CMI

Polyreactive stimulation – ELISpot-T IFN- γ (anti-CD3)

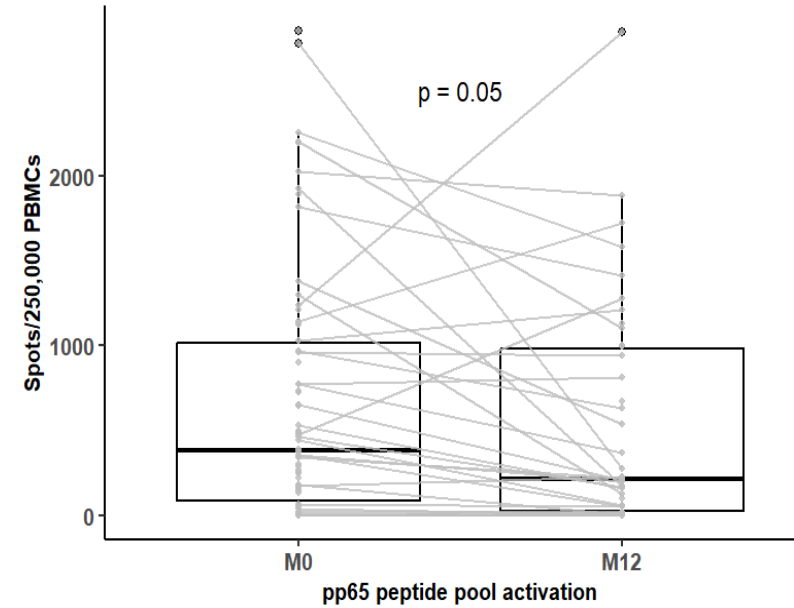
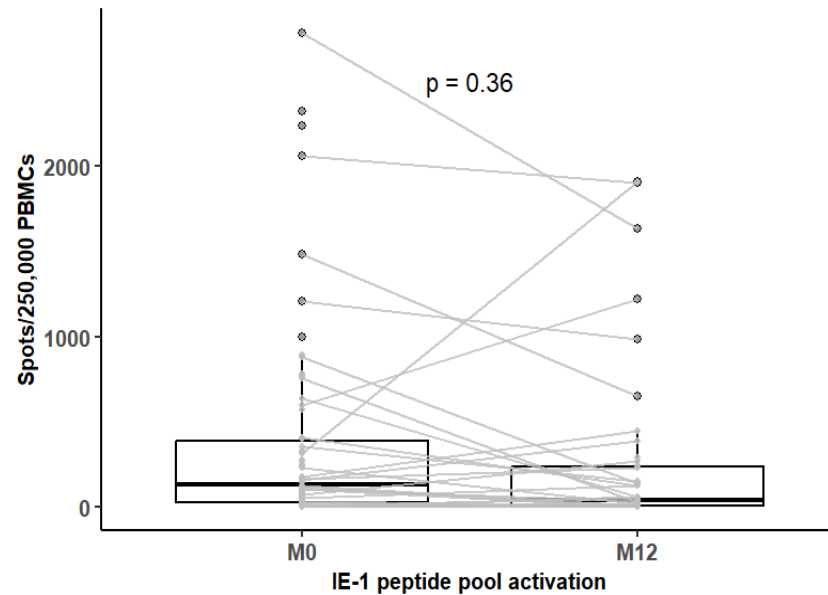


The **first study** evaluating CMI response in belatacept-treated recipients



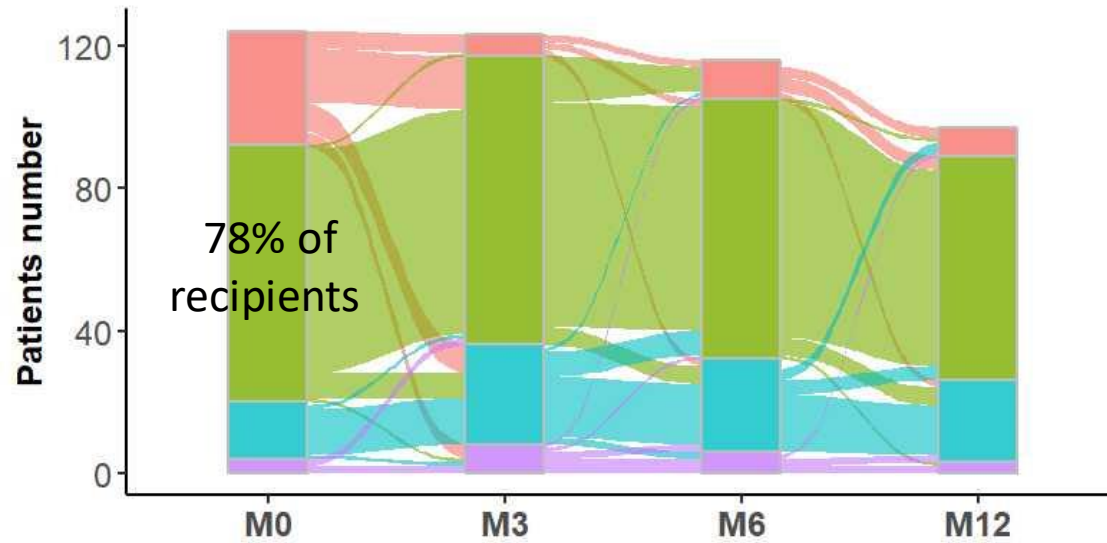
- **Significant decrease of CMI response after polyreactive stimulation**
- Factors influencing : Delay between **belatacept-conversion and the transplantation** ($p < 0,05$)
Age the day of the conversion (Decrease only in patients < **59 years old**)

Results : impact of belatacept-conversion on CMV-CMI



- Concordance between ELISpot-T and CMV serology
- **Decrease of CMI response after specific CMV stimulation**, EBV ($p = 0.68$) and BKV ($p=0.05$) stimulation
- No relation between CMI response and belatacept concentration

Results : TTV load at baseline and opportunistic viral replication



Alluvial plot of the number of patients in the categories

- Only one patient presented a rejection
- To date : low number of viral replication during follow-up and, no CMV disease
 - TTV load : no predictive of viral replication

Risk stratification (*Haupenthal et al. European TTV Guide study, 2023*)

- 4.6 – 6.2 log cp/mL – no risk
- < 4.6 log cp/mL – rejection risk
- > 6.2 log cp/mL – infection risk
- NA

- *Bertrand D et al.*,
early conversion → increased risks of rejection & opportunistic infections (median time = 6 months)
- *Fernandez-Ruiz et al.* study
TTV load was higher at 1 month post transplant in patients presented BKV viremia

DISCUSSION / CONCLUSION

No impact of belatacept-conversion on TTV load

TTV load threshold
recipients on tacrolimus (*Haupenthal et al. European TTV Guide study, 2023*)



TTV load threshold
recipients on belatacept

Decrease of CMI response after belatacept-conversion

- Explain why belatacept therapy was associated with an increased risk of CMV disease and severe CMV and BKV viremia (*Bertrand et al. 2020, Benefit study 2010*)
- Significant increased of EBV load between M0 and M12 (1.41 to 2.48 log cp/mL)

Further studies → impact of belatacept on IFN- γ secretion ?

No impact of through belatacept concentration & TTV load / CMI response

Further studies → need of belatacept concentration monitoring?

Merci pour votre attention

**Equipe technique et biologique du
laboratoire de virologie**

Etudiants :

L. Cabezas

L. Fusillier

B. Nicolas-Truphemus

M. Gnesotto

Equipe de la **DRCI** et Dr Marc
Manceau (CIC)

Le service de **Néphrologie**
(Dr J. Noble, Pr T. Jouve)

Dr H. Mohammed

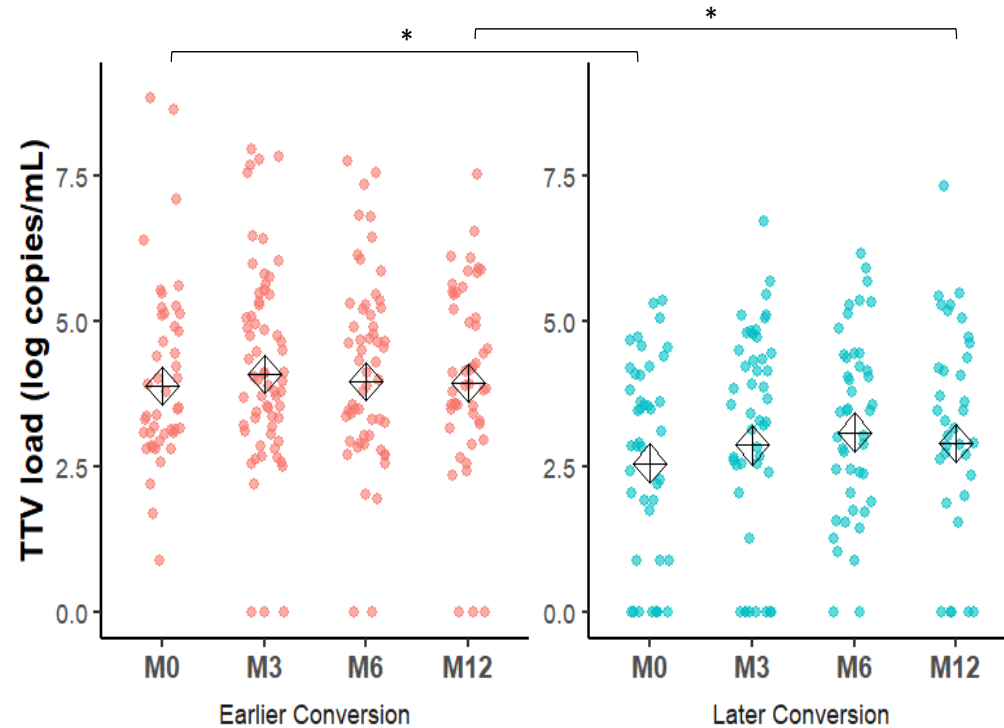
Laboratoire **bioMerieux**

Equipe de **Mabtech**

Mes co-directeurs de thèse :
Pr Germe et Pr Jouve



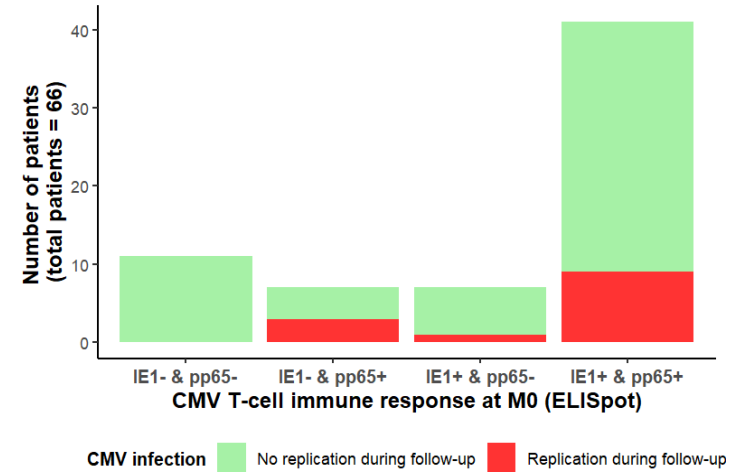
Results : factors influencing TTV load post-conversion



- **Impact of delay between belatacept conversion and the transplantation**
 - ✓ Patients with belatacept-conversion before 4 years after transplantation → higher TTV load
- Patients with **age > median (59 years old)** increased TTV load from M0 to M12

Results : TTV load at baseline and opportunistic viral replication

N = 20 patients with CMV replication
→ 9 at low risk at baseline

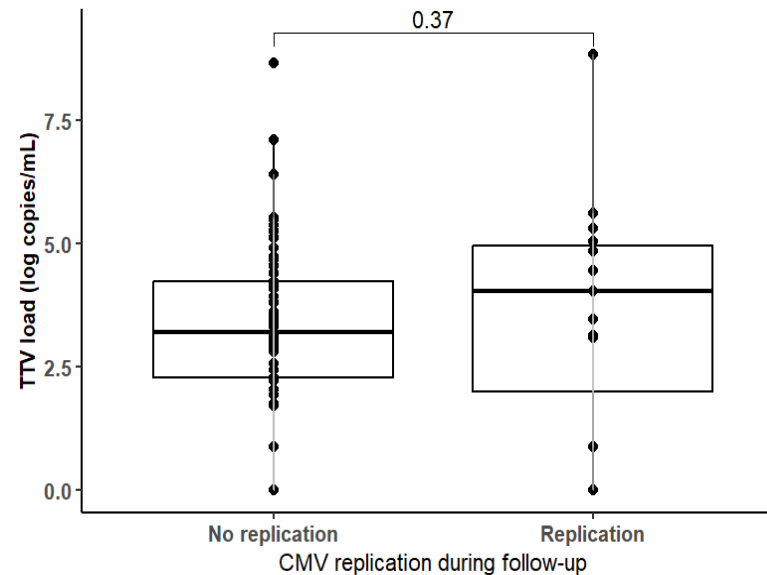


Cutoff:

IE-1 > 25 spots/250,000 PBMCs pp65

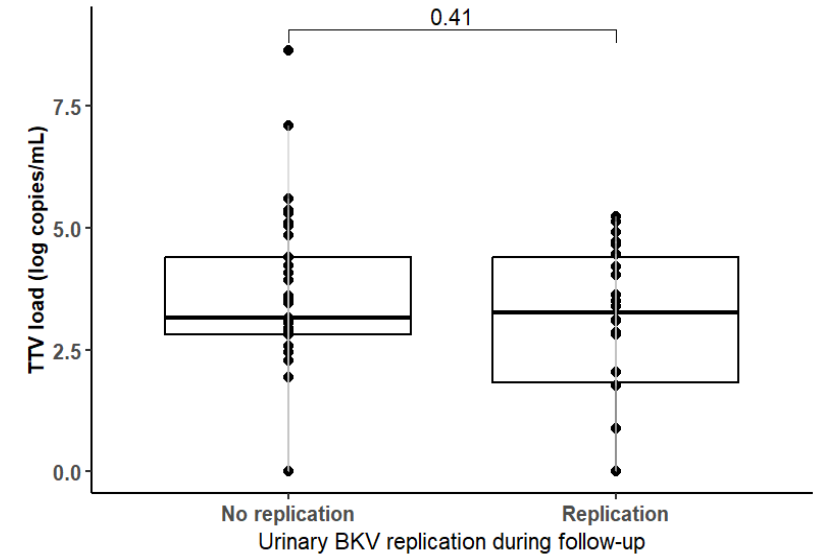
> 30 spots/250,000 PBMCs

Jarque M, transplantation, 2018



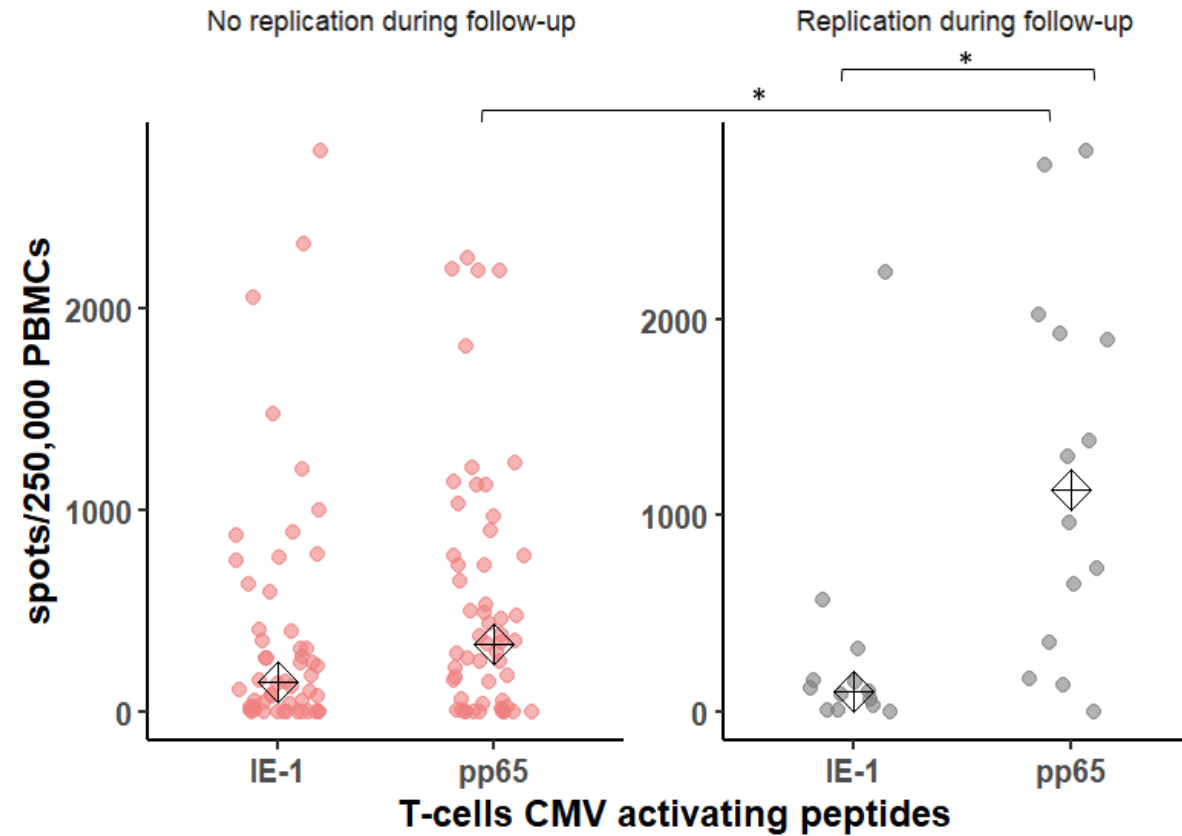
3.6 log versus 3.2 log copies/mL

N = 44 patients with urinary BKV replication

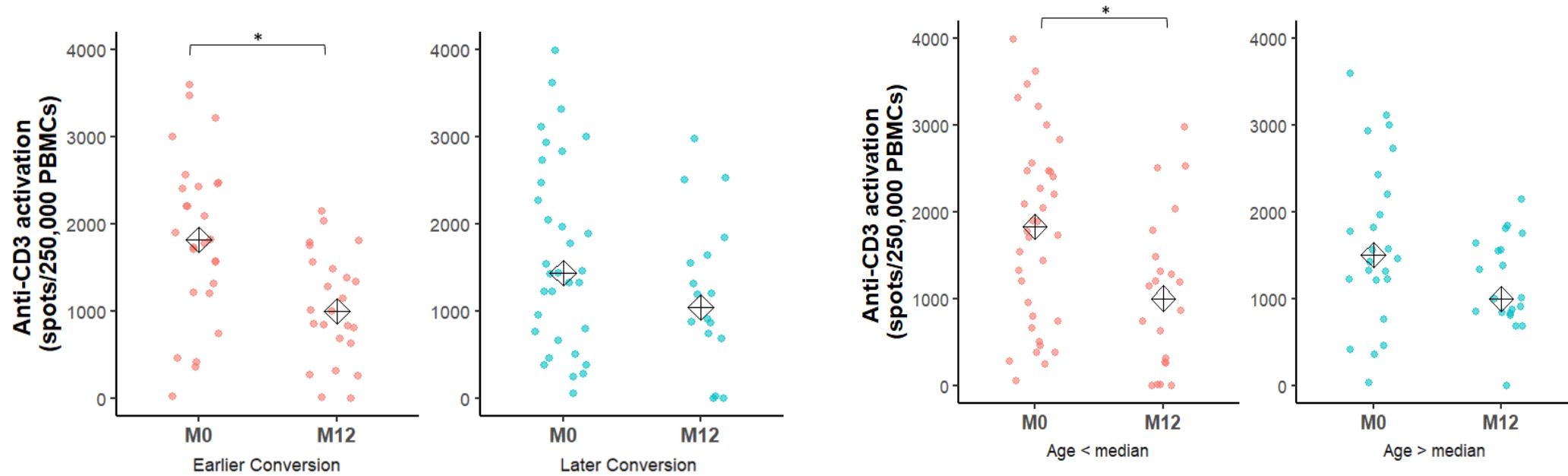


2.9 log versus 3.5 log copies/mL

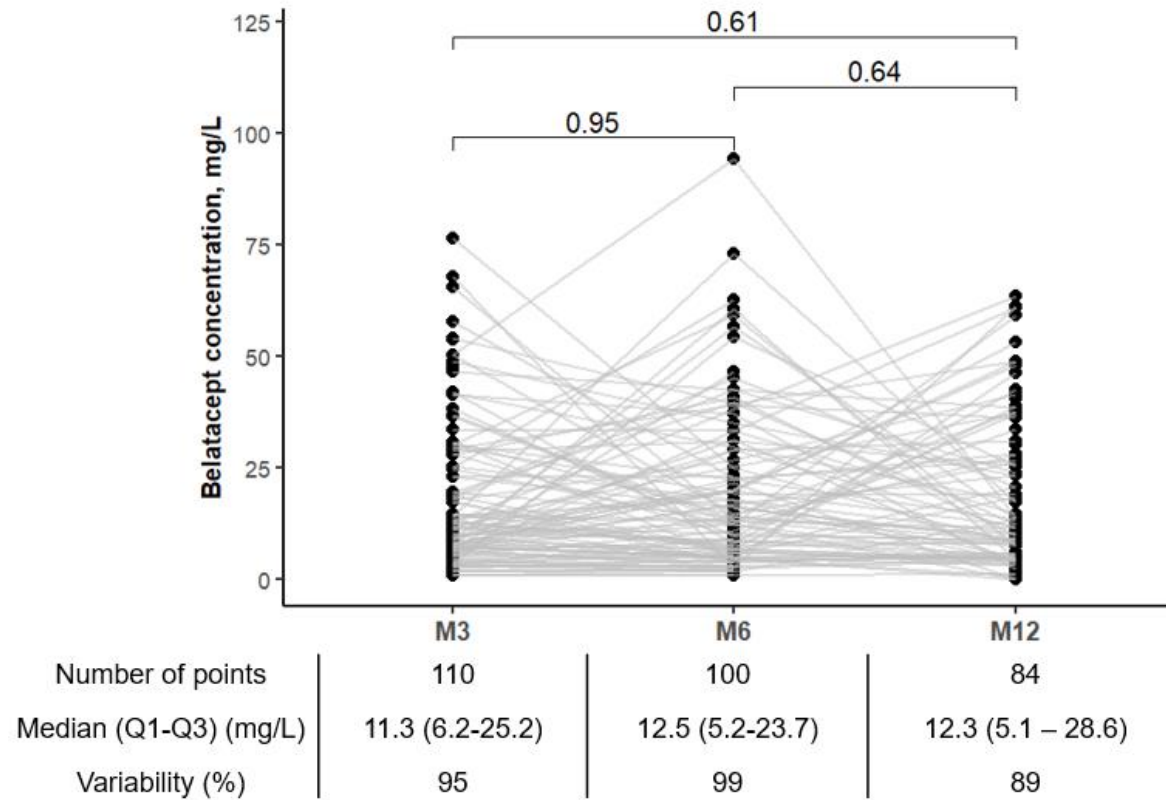
Results : T-cell immune response at baseline and CMV replication



Results : factors influencing CMI modification



Results : Monitoring of belatacept concentration



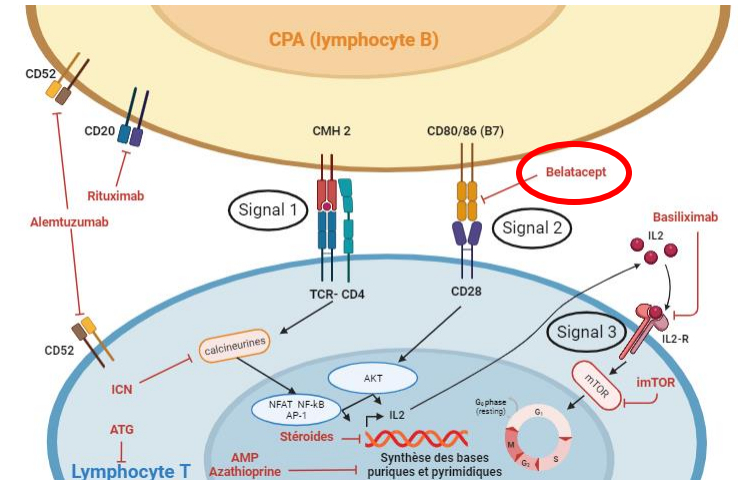
- Intra-individual variability = 52%
- Inter-individual variability = 94%

Context

Immunosuppressive based therapy : tacrolimus switch to Belatacept



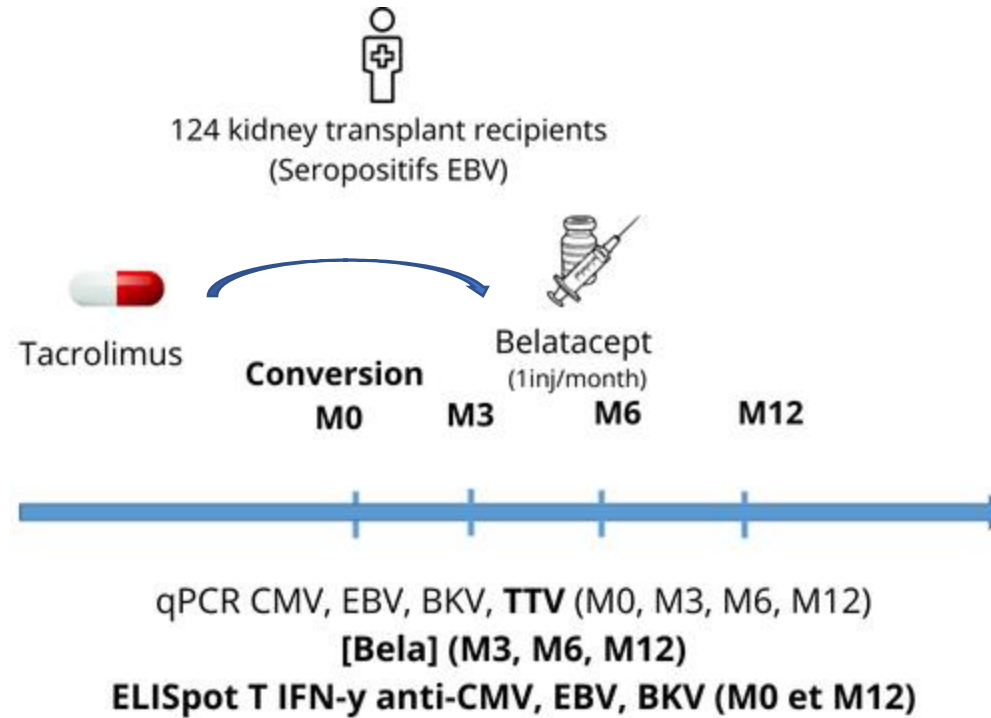
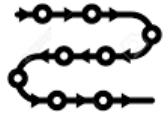
To improve adherence, metabolic parameters, renal function



Current challenge :

Impact of a tacrolimus-to-belatacept conversion on the TTV load and CMI response

Material & Method



Retrospective study, monocentric



- Evaluation of the impact of the conversion to belatacept on TTV viral load
- Evaluation of the impact of the conversion to belatacept on CMI
- Analyze the relationship between these 2 biomarkers and opportunistic infections/rejection after 1 year of belatacept treatment